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TROPICAL DISEASES BULLETIN

VOL. 38.] 1941. [No. 11.

IMPERIAL MYCOLOGICAL INSTITUTE 1941

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Issued under
the Direction of the
Honorary Managing Committee of the
BUREAU OF HYGIENE AND TROPICAL DISEASES,
Keppel Street, London, W.C.1.

Price 2/6 Net.] *Entered as Second Class Matter in the U.S.A. Post.* [Annual Subscription 21/- With Supplement 25/-

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BUREAU OF HYGIENE AND TROPICAL DISEASES.

TROPICAL DISEASES BULLETIN.

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SUMMARY OF RECENT ABSTRACTS.*

IX. LEPROSY.

Epidemiology.

MONACELLI (p. 48) states that there are several endemic foci of leprosy in Sicily, and has described the new leprosarium at Messina.

MUIR (p. 328) reports on leprosy in Southern Africa. It is common in the hot, damp, low-lying areas around Lake Nyasa and in the basin of the Zambesi. In South Africa a severe type is seen in Europeans, but the numbers are decreasing. BRIERCLIFFE (p. 624) estimates the number of lepers in Nigeria as 200,000, or at least 1 per cent. of the population: this number is probably exceeded only in India and China. The Commission on leprosy in the Belgian colonies (p. 637) states that in the Congo 60,363 cases have been found.

BOENJAMIN (p. 627) estimates that there are at least 1,000 lepers in Batavia, representing an incidence of 2 per 1000.

DELINOTTE (p. 636) states that in the French colonies there are 104,000 known cases and it is estimated that 170,000 further cases exist.

In Brazil, BARRETO (p. 637) states that there are 35,241 known cases. There are 41 dispensaries, and the institutions now existing or planned will enable 24,888 patients to be accommodated. MALDONADO ROMERO (p. 330) calculates the incidence of leprosy in Colombia as 1·92 per thousand of the population. In Sotomayor, Colombia, GEORGE (p. 330) states that the incidence is 3·6 per 1,000, and the number of cases is increasing; it is believed that dietary deficiency is an important contributory cause.

In the report of the Saidapet Health Project (p. 625) the importance of contact with open cases is stressed; in one village every definite case was shown to have had contact with an open case, but it is pointed out that the whole village may be regarded as one family group.

* The information from which this series of summaries has been compiled is given in the abstracts made by the Sectional Editors in the *Tropical Diseases Bulletin*, 1940, Vol. 37. References to the abstracts are given under the names of the authors quoted and the pages on which the abstracts are printed.

AUSTIN (p. 626) shows that in the Fiji islands the incidence of leprosy depends essentially upon the density of the population ; by means of a genealogical tree he has traced 58 lepers in one family group.

Aetiology.

LIMA and ARANTES (p. 332) state that they have obtained growths of *Myco. leprae*, from human material, in Sauton's medium, failing only twice in 36 attempts. From microscopic examination of the growths they claim that the organism passes through various phases. GAVRILOV and FESTER (p. 333) report success in the cultivation of the bacillus of rat leprosy in animal tissue culture.

MANALANG (p. 332) reports on a study of the morphology of *Myco. leprae* in human tissues. The interpretation of the granular forms, and the significance of the predominance of a certain form in a lesion, remain a matter for conjecture.

BURNET and JADFARD (p. 331) have apparently succeeded in infecting a hamster by feeding it on leprosy material daily for 12 days. DOULL and MEGRAIL (p. 627) record success in infecting a Syrian hamster with material from a human case. LAIDLAW (p. 628) found that after hamsters had been infected from human material obtained from the Belgian Congo, material from their lesions, when inoculated into other hamsters and into white rats, produced rapidly spreading infection. This fact, together with observations on the tissues of the animals, suggested that the lesions from which the material was originally obtained were due to infection with the organism of rat leprosy and not to the usual human type, though the appearances in the original patient had aroused no suspicion of origin from the rat leprosy bacillus. The possibility that human leprosy originated from the more prevalent rat leprosy is discussed.

COCHRANE *et al.* (p. 331) report experiments in which material from human nodular lesions was inoculated into monkeys from which the spleens had been removed. The results were inconclusive, but reveal the possibility of individual resistance.

OTA and SATO (p. 628) found results in hens inoculated with human or rat leprosy bacilli which indicated that multiplication had taken place, together with more characteristic macroscopic and microscopic changes than are found in other experimental animals.

MARCHOUX and CHORINE (p. 49) show that rat leprosy bacilli cannot penetrate the skin of rats after simple depilation, in which the roots are left intact, but that if the hairs are pulled out they can penetrate through the small wounds thus formed.

Pathology.

RODRIGUEZ *et al.* (p. 630) report lepromatous changes developing in three cases of macular leprosy.

ERMAKOVA (p. 629) has described the histopathology of anaesthetic patches, depigmented macules and tuberculoid lesions. In all there was chronic inflammatory change with polyneuritis.

SÁENZ and PALOMINO (p. 39) give a description of tuberculoid leprosy, which can only certainly be recognized by microscopical examination. Anaesthesia is a constant symptom in parts of the skin lesions, and the bacilli may be absent or very scarce. WADE *et al.* (p. 631) discuss the course of tuberculoid leprosy, showing that there is

no fundamental type differentiation between the major tuberculoid lesions and those of the lesser forms of neuromacular leprosy. Spread may take place by extension and not necessarily by metastasis, but there may be a secondary eruption, papular or macular, which is apparently due to metastatic dissemination. LOWE (p. 39) has found tuberculoid changes in lymph glands in leprosy. SCHUJMAN (p. 39) regards tuberculoid leprosy as a manifestation of the allergic state, and has not seen any case in which this form has become lepromatous. The Mitsuda test is positive in tuberculoid and negative in lepromatous cases. STEIN (p. 631) also considers that tuberculoid changes are the expression of a peculiar allergic condition, accompanied by strongly developed immunity, and occur when the course of the disease is benign.

MUIR (p. 333) discusses resistance in leprosy. Natural resistance is inborn in most subjects, but is low in children; it does not appear to vary much in families or races. General resistance is in proportion to general health; acquired resistance may be systemic or local.

Clinical.

MUIR (p. 41) discusses the mental changes brought about in lepers by the attitude adopted to them by the general community.

RODRIGUEZ and WADE (p. 338) have studied the progress of 46 neural cases, in which little or no treatment was given, during a period of 5 years. In 33 the original lesions had either disappeared or improved, but the authors consider that still better results would have been achieved with regular treatment. They also refer to two cases of tuberculoid leprosy in which reaction occurred after a long quiescent period or after apparent recovery. RISHI (p. 339) reports a higher rate of relapse in lepromatous (18·0 per cent.) than in neural cases (8·5 per cent.) in India, among a group of arrested cases observed over long periods. The chances of relapse beyond 10 years of arrest appear to be small.

BECHELLI (p. 41) records a case of leprosy in which the condition started in the form of polyneuritis with involvement of the sciatic and popliteal nerves and the brachial and cervical plexuses.

DE BARROS (p. 40) discusses the eye lesions found in leprosy. There is parallelism between corneal and skin lesions, with infiltration, nodule formation, or both. In the iris there may be diffuse inflammation or miliary nodules, and the characteristics of these two forms are described.

GERMOND (p. 338) discusses the differential diagnosis of circinate tuberculoid leprides and polycyclic syphilides. CAMPOS and ALAYON (p. 42) also note the resemblance between certain syphilides and leprotic lesions, particularly tuberculo-circinate lesions of the skin.

MUIR (p. 340) points out that Epidermophyton infections are troublesome complications of leprosy and that the loss of sweating power predisposes to them. He gives details of a treatment advised.

RYRIE (p. 337) has found that plantar hyperalgesia is a useful early sign of the leprosy reaction and describes his method of eliciting it. It is associated with high sedimentation rate and a high proportion of positive findings on examination of thick blood films; it therefore appears to be an indication of progressive disease.

STEIN (p. 334) describes inflammatory changes of a hyperergic type, with necrosis and suppuration, in lepromatous granulomata during the course of the lepra reaction.

NÚÑEZ ANDRADE (p. 42) has tabulated the principal causes of death in lepers in Mexico and at Culion. In Mexico enterocolitis and leprotic cachexia are the most common ; at Culion, on the other hand, pulmonary tuberculosis, nephritis and bronchopneumonia head the list. The facts are recorded ; no explanation is attempted.

MANALANG (p. 630) found 28 per cent. more positives by using the Cooper modification of the Ziehl-Neelsen staining technique than by the ordinary method.

ROTBERG (p. 43) discusses the lepromin test and the criteria on which it may be regarded as positive. In the nodular form it is negative, but a non-specific papular reaction, reaching its maximum before the fifth day, and persisting sometimes to the fourth week, may be seen and should not be confused with a true positive. In the tuberculoid form the true positive reaction occurs, reaching its maximum from the second to the sixth week and often suppurating. FERNANDEZ (p. 632) similarly states that with the lepromin test there is an allergic reaction which may be seen after 48 hours, as well as the late result in the third or fourth week. In 95 per cent. of cases the early and the late reactions agree, though they are probably produced by different fractions of the leprosy bacillus. A filtrate of lepromin always gives the early reaction in allergic cases, but rarely the late reaction, and then only faintly. MENDES and GIL DE CASTRO CERQUEIRA (p. 336) find that the active fraction of lepromin is the non-filterable constituent, and that different preparations vary greatly in activity, so that standardization is necessary.

LARA (p. 335) has investigated the lepromin test in children of leprous parents ; the impression was gained that it is of no value as an index of resistance in children over one year, that it has no prophylactic value in such children, and that there is a possibility that it may act provocatively.

LAGROSA (p. 335) found, in a series of lepromin tests in bacteriologically negative lepers, that the proportion of negative reactors steadily diminished as the tests were repeated. At the fourth test all gave positive results. Similarly, in bacteriologically positive cases, IGNACIO (p. 335) found that whereas only 21 per cent. were positive to the first test, the proportion had risen to 80 per cent. at the fourth. The reactions could not be correlated with the clinical changes. LARA (p. 632) found that, contrary to earlier statements, the lepromin test may be positive in children below one year of age, and that if the test is repeated every four months most children of lepers give positive results. Early lesions in the children were associated with undiminished tendency to react positively, and the duration and constancy of exposure to infection appeared to bear a direct relation to the proportion of positive reactions.

BLACK and ROSS (p. 42) have examined lepers and non-leprous controls by the complement fixation test of Lleras Acosta, and conclude that, because of the few positive results obtained in neural leprosy and the relatively large number of positive controls, the test is of no practical value. RADNA (p. 336) regards the Witebsky-Klingenstein-Kuhn reaction as of diagnostic value in bacteriologically negative neural leprosy. He (p. 337) considers that the Wassermann reaction is only positive if syphilis is present. MONTEL *et al.* (p. 43) have not found the Vernes flocculation reaction to be of value in the diagnosis of leprosy.

JUSCHKO (p. 44) has found that in leprosy the absorption of saline injected intradermally is more rapid than in normal persons. This test is of some value in determining the general state of the patient.

DHARMENDRA (p. 337) confirms earlier findings that there is a shift to the left in the Arneth count in leprosy.

Treatment.

BEAUDIMENT and RIVOALEN (p. 340) state that chaulmoogra oils should show not more than 6 per cent. acidity for oral use, 3 per cent. for intramuscular or subcutaneous use, and 0·8 per cent. for intravenous use. Neutralization does not diminish the activity of the oils, and the authors describe a simple method of effecting neutralization. PAGET *et al.* (p. 45) discuss the irritant action of some hydnocarpus preparations.

DUBOIS and RESSELER (p. 340) describe an emulsion of chaulmoogra oil, of which they give a good account in treatment. For intravenous use RADNA (p. 342) employs a mixture of 7 parts chaulmoogra oil and 3 parts of a 3 per cent. solution of gynocardate of soda. For intradermal use he mixes chaulmoogra oil with 2 per cent. creosote.

MOISER (p. 633) analyses the results of treatment with a number of preparations, and indicates that in his cases Moogrol gave the best results.

GRIMES (p. 46) reports excellent results from the use of fluid and alcoholic extracts of the dried plant *Hydrocotyle asiatica*, given by the mouth. This treatment is most effective in lepromatous cases, but is also useful in neural leprosy.

ETCHEVERRY (p. 46) writes of the value of injections of bile salts, dissolved in saline, in treatment. For lepromata he injects solutions of 2–3 per cent. into the nodules; these cause reactions which gradually subside and permit of repetition in 8–10 days. For eye lesions solutions of 0·5–1 per cent. are used as baths or are injected subconjunctivally (in which case the diluent is isotonic glucose solution), or an ointment of the same strength may be applied. He claims good results by these means.

Discussing the treatment of leprosy, DELANOE (p. 44) advocates the constant changing of drugs so that the bacilli cannot become accustomed to any one; he claims good results and gives a list of the drugs used.

GMINDER (p. 333) considers that vitamin deficiency predisposes to leprosy infection, and records considerable success in the treatment of generalized leprosy with Betaxin, the synthetic crystalline vitamin B_1. HOU (p. 635) shows that in leprosy the urinary excretion of vitamin B_1 is far below normal but may be raised by oral administration. He therefore advises that vitamin B_1 should be given especially in cases in which neuritis is present. BLUETH (p. 47) reports useful results, in vaso-dilatory symptoms due to nerve lesions, after treatment with Betaxin.

Gold treatment has been used by ZANETTI (p. 634) and DE GOLOVINE (p. 634), who report favourably on its effect on the general health.

IRVINE (p. 342) reports unfavourably on sulphapyridine in leprosy.

BOENJAMIN (p. 46) reports on the treatment of 7 patients with Reenstierna's antileprosy serum, but makes it clear that the series is too small for definite conclusions to be drawn.

JOHANSEN (p. 343) reports very unsatisfactory results in the treatment of leprosy by means of the Kettering hypertherm.

COCHRANE *et al.* (p. 342) report success in the treatment of lepra reactions with fouadin, which is less toxic than tartar emetic. GERMOND (p. 635) also uses fouadin for the treatment of lepra reactions and has had success with sulphonamide drugs for the same purpose. RADNA (p. 47) states that blood transfusion is useful in the treatment of lepra reactions.

In the *International Journal of Leprosy* (p. 343) are collected records of the surgical removal of solitary leprids in 19 cases; there was no relapse in 12, but it is pointed out that such slight lesions often yield readily to medical treatment. DHARMENDRA and CHATTERJI (p. 343) found local relapse in 3, and general relapse in 1, of 18 cases in which early neuro-macular lesions had been excised, but the period of observation was too short to allow of definite conclusions.

COCHRANE (p. 635) gives details of the treatment he uses for trophic ulcers, and RYRIE (p. 636) refers to the excellent effect of dressings containing vitamin A on the ulcers of leprosy, giving details of the preparations used, which include shark liver oil. VESPOLI (p. 341) gives details of the treatment he uses for the ulcers of leprosy.

Since deformities of the hands and feet in neural leprosy are largely the result of paresis of the intrinsic muscles, OBERDÖRFFER and COLLIER (p. 47) advocate daily exercises to restore function; they give a formula for dressings to be used on ulcers.

Control.

In South Africa, MUIR (p. 328) reports that the compulsory system has been modified to allow uninfective and recovered patients to be released, and that as a result good progress is being made. The Emjanyana institution in the Transkei is becoming so popular that more than one-third of the admissions are voluntary and these patients insist on receiving the compulsory treatment, with gratifying results. In Basutoland a compulsory system is in force, one feature of which is the training of leprosy inspectors to search out the cases.

BRIERCLIFFE (p. 624) states that in Nigeria there are now 14 settlements in 23 provinces, and that the voluntary system of segregation has proved to be a great success. In the same country, MUIR (p. 328) reports that although compulsory segregation is impossible for financial reasons, a great deal has been done at small expense through the co-operation of missions with the Government. The Uzuakoli settlement has recently extended its work by establishing clinics in the surrounding villages. DAVEY (p. 48) describes the Uzuakoli leper colony in Nigeria, where 25 leper nurses have been trained to help in the work. Agriculture and industry are being developed and the colony is becoming more self-supporting. In the villages of the district the inhabitants are encouraged to segregate their cases locally and where this is done treatment is given each week by members of the Uzuakoli staff who visit the villages. By this means large numbers of patients are reached and contacts are known and observed. LANGAUER (p. 624) also comments on the success of the survey-propaganda-treatment system in Nigeria, as a result of which the Ossiomo settlement has become very popular.

DELINOTTE (p. 636) describes the measures taken to control leprosy in the French colonies. These consist principally of registration,

isolation in institutes of crippled or infective patients, and treatment of closed non-infective patients in their homes. Propaganda is provided for. In the Belgian Congo (p. 637) 14,983 lepers are isolated in leprosaria of the agricultural colony type, and 3,000 in villages or camps. MUIR and CHATTERJI (p. 328) report on surveys carried out in a village in Bengal, from which it is deduced that voluntary home isolation of infective lepers was effective in preventing spread of infection over a period of 5 years.

AUSTIN (p. 626) reports on the working of the compulsory system at Makogai, Fiji, and states that in agricultural institutions the co-operation of the patients may be obtained without any sense of grievance. He stresses the importance of the examination of family contacts.

LLERAS RESTREPO (p. 344) urges the establishment of many more preventoria for the healthy children of lepers in Colombia. One has already been started but will maintain only 150 of the 2,000 healthy children in the leprosaria of the country.

In the opinion of MANALANG (p. 48) leprosy is acquired chiefly, if not entirely, in childhood, and adults may be considered immune. [This may be true of indigenous peoples, but that it is not universally true is suggested by the investigations of ARAUJO and DE ALBUQUERQUE (this *Bulletin*, 1941, Vol. 38, p. 458) who found that adult immigrants to Brazil are as susceptible as Brazilian children.] Manalang therefore proposed a scheme in which adult lepers, in the Philippines, who wish to return home may do so, the money thus saved being used to isolate in government homes the children born to lepers. The council of Hygiene, Manila, could not, however, accept this extreme view, and expressed a preference for the proposals made at the Cairo Congress.

Charles Wilcocks.

PLAGUE.

PRÉCIS of ABSTRACTS IN THIS SECTION.

In the Annual Report of the League of Nations Eastern Bureau (p. 619) it is stated that in tropical countries plague tends to die out in lowlands and to spread to the cooler climate of mountain regions. Plague in India is briefly reviewed from 1900 onwards. In Java the recent remarkable decline in mortality is ascribed to house improvement and to the use of the Otten vaccine. In ports, prime importance is attached, not to the total number or species of fleas, or the number of infected fleas, but to the number of infective fleas, and this may depend entirely on climatic conditions.

RAO (p. 620) has endeavoured to find the cause of the relative immunity of Calcutta from plague by making a rat-flea survey, in which he found that the flea indices are quite favourable to the spread of the disease in epidemic form. No explanation, therefore, of the rarity of plague is yet available. GEORGE and TIMOTHY (p. 621) examined rodents in a plague area in the Nilgiris, S. India, but found plague in *R. rattus* only ; there was no proof of the existence of sylvatic plague, but the enquiry is only in its preliminary stages. Of the fleas

found on field rats, Stivalius and *Nosopsyllus nilgirensis* are capable of transmitting plague. MAKAND (p. 621) reports on plague in the Central Provinces of India during 1939.

DAVIS (p. 622) states that plague is now enzootic in the rodent population over a large area of S. Africa. Human cases occur, and it appears that *Mastomys coucha* and *R. rattus* now form reservoirs independent of gerbilles. A list is given of the principal fleas found on gerbilles and on *R. rattus*. The numbers of fleas in the burrows are controlled mainly by climatic conditions which fluctuate with the seasons. The numbers of fleas found on rats give no indication of the flea population of the burrows, and the author describes his method of counting the fleas in the burrows. VAN HOOF (p. 623) reports two foci of sylvatic plague in the Belgian Congo. In one *R. rattus* is absent but many other rodents are found, in the other *R. rattus* is present.

In *Public Health Reports* (p. 623) is a record of a case of plague, probably sylvatic in origin, in the United States. ACKERT *et al.* (p. 623) show that *X. cheopis* can overwinter on *R. norvegicus* in Kansas, and is established there. Sylvatic plague is spreading eastwards and the field rodents may infect *R. norvegicus*, against which measures should be taken.

MACCHIAVELLO (p. 624) states that in the north-east of Brazil rural plague is not primarily a disease of wild rodents, but is only epizootic in rats, especially *Rattus rattus*. It is spread by *Xenopsylla cheopis*, which tends to leave rat nests only in the cool season, and may transmit the disease to field mice and thence to wild rodents. He points out that in outbreaks of human plague associated with epizootics due to other organisms it may wrongly be assumed that the epizootics are due to plague. He describes a new syndrome stated to be due to plague.

D'AMATO (p. 624) names the places at which plague has recently been found in the Argentine. PARDAL (p. 625) reports a case of plague, probably sylvatic in origin, from that country. MOLL and O'LEARY (p. 625) state that in Chile plague is restricted almost entirely to ports. The climate south of Valparaiso seems to be unfavourable to *X. cheopis*, and in the north the ports are surrounded by dry country with few rats and no fleas.

HARALSON (p. 626) reports that Hawaii is still a centre for plague though it has disappeared from Oaku and Mani.

KAMAL (p. 626) writes of plague in Egypt, and reports that in children enlarged glands, due to plague, are commonly seen in the absence of any other symptoms. In vaccinated persons he reports a case mortality of 25 per cent., in unvaccinated of 34·3 per cent. Treatment with large doses of serum gives good results. KAMAL *et al.* (p. 626) in Egypt do not entertain a high opinion of vaccination as a means of arresting an epidemic of plague, though they think that the fatality rate in bubonic plague is distinctly lower in the vaccinated than in the non-vaccinated. They refer to the spread of the disease by the faeces of pigeons, living in rat-infested houses, which are used as manure. In treatment they advise serum with sulphapyridine.

MURDOCK (p. 627) refers to three outbreaks of plague in which the pneumonic form developed in cases of bubonic disease, and to the danger of direct transmission of the pneumonic form. He describes the clinical progress and the steps which should be taken to protect attendants and to isolate the cases and their contacts.

Junior and de Albuquerque (p. 628) describe a skin test for plague in which an antigen from an infected lymph gland is used. The reaction appears to be valuable in retrospective diagnosis.

Wagle *et al.* (p. 628) report on the treatment of 237 cases; serum, sulphapyridine and sulphathiazole each gave considerably better results than intravenous iodine, but there is little to choose between the three first-named methods except that in septicaemia serum cannot be given in sufficient quantity because of the shock produced. Chopra *et al.* (p. 629) report the successful treatment of a case of plague with sulphapyridine.

In the *Journal of the Egyptian Public Health Association* (p. 629) are given the measures taken to diagnose deaths due to plague and to deal with outbreaks.

Hopkins (p. 629) describes the anti-plague measures taken in Uganda. *C. W.*

Severn (A. G. M.). **Plague.**—*Med. Press & Circular.* 1941. July 23. Vol. 206. No. 4. pp. 74–77.

This is a brief general account of plague, particularly in the East. Though there is nothing new in this paper to readers of this *Bulletin*, recent work on the subject is mentioned, particularly treatment with sulphonamides and prevention by living avirulent vaccine and by improved construction of buildings. *C. W.*

League of Nations. Health Organisation. Eastern Bureau, Singapore. Annual Report for 1940. pp. 6–37. With 18 graphs & 2 maps. [11 refs.]—**Disease Incidence :—(A) Plague (General). (B) Plague in Countries. (C) Plague in Sea and Air Ports.**

(A) *Plague (General).*—The spread of plague to other ports from Hong Kong in 1904 aroused attention to the possibilities of its dissemination by maritime trade. Expectations were not altogether borne out by experience and the explanation given, for tropical and semi-tropical countries, is that plague tends to die out in lowlands and to spread inland where it may find an endemic home in the cooler climate of mountain regions. The history of plague spread in Java and in Madagascar confirms this point of view.

(B) *Plague in countries.*—The countries referred to are British India, Netherlands Indies, Thailand, Burma and China. Some very interesting graphs and maps are presented. In graph No. 1 the plague, cholera and smallpox deaths from 1900–1939 in British India are shown. This graph shows, and especially by contrast, how plague deaths have fallen in this period of time. They were 3,911,903 for 1900–04 and only 116,792 in 1935–39. Another interesting analysis relates to the incidence of plague in British India from 1924–38. Individual provinces showed marked differences, favourable for the Punjab and Bombay, but not so favourable for the United Provinces. "The outstanding features in this period . . . are :—(1) the fall in mortality of the country as a whole ; (2) the severe mortality in Punjab in 1924 and 1926, followed by its marked decrease and ultimate disappearance, and (3) the steady mortality in United Provinces in the latter ten years of the period." The Netherlands Indies (Java) record a phenomenal decrease in plague deaths from 1934–1940. Two

entirely different methods of control are regarded as being responsible for this :—(1) thorough and systematic large scale improvement of 1½ million houses between 1911 and 1938, (2) the introduction of mass inoculation by Otten's live non-virulent vaccine in 1935. China had reason to be concerned with the existence of plague in Burma, owing to the traffic on the Yunnan-Burma road. The National Health Administration of China seems to have the situation well in hand. "Fortunately Lashio has so far remained free from plague" and the Government of Burma may establish "additional quarantine stations . . . to watch the traffic on caravan routes."

(C) *Plague in sea and air ports.*—Much consideration is given to the transmission of plague by fleas especially where voyages are comparatively short. "It appears that it is not the total number of fleas or the specific flea counts that matter, not even the number of infected fleas, but the number of infective fleas that is of prime importance, and this depends perhaps entirely on climatic conditions." Plague seasons for different ports do not necessarily correspond.

W. F. Harvey.

Pasricha (C. L.) & Panja (G.). **A Search for Latent Sylvatic Plague in Calcutta.**—*Indian Med. Gaz.* 1941. Apr. Vol. 76. No. 4. pp. 212–213.

The importance of sylvatic plague needs no emphasis. It may exist for a long time as an inapparent, invisible infection and the authors have considered it advisable to start a search for this latent plague in Calcutta. Only 200 rats have, so far, been examined "with negative results for *P. pestis.*" *W. F. H.*

Rao (S. Raghvender). **Rat-Fleas of Calcutta : investigated from a Point of View of Epidemiology of Plague.**—*Indian Jl. Med. Res.* 1941. Jan. Vol. 29. No. 1. pp. 51–70. With 1 graph. [14 refs.]

The comparative freedom from plague of Calcutta as compared with Bombay has always been puzzling. The present investigation has been a thorough one of several wards and has been directed especially to the species of flea infesting rodents and to the flea indices. The types of ward selected were those with : (1) high incidence of plague, (2) low incidence of plague, (3) high density of population, (4) low density of population, (5) mostly indigenous population, (6) mostly foreign population, (7) business quarters, grain godowns, etc., (8) mostly residential quarters, (9) wards with sewers, (10) a ward without sewers, and (11) the port area. This choice was considered to give "a complete representative sample of all the environmental and topographical conditions of the city." As a result of the investigation the author concludes that previous explanations of the relative absence of plague in Calcutta, as due to the paucity of fleas or to a flea species factor, are not acceptable. This survey has shown for example that *X. cheopis* forms a fairly high proportion of the rat-flea population and in some wards even outnumbers *X. astia.* Nevertheless of the 4,888 fleas collected 60·6 per cent. belonged to the species *Xenopsylla astia* and 39·4 per cent. to the species *Xenopsylla cheopis.*

It was also found that " *Rattus rattus* carried more cheopis than astia, while the reverse was the case with *Rattus norvegicus* and *Gunomys varius*." No explanation is forthcoming of the immunity of Calcutta from plague, but it is laid down that :—" Compared with other Indian cities Calcutta possesses high general and specific flea indices and this flea factor is quite favourable for the spread of plague in an epidemic form provided the other factors concerned in the epidemiology of plague are also favourable." *W. F. H.*

George (P. V.) & Timothy (B.). **A Preliminary Study of Plague at a Hill Station in the Nilgiris, South India.**—*Indian Med. Gaz.* 1941. Mar. Vol. 76. No. 3. pp. 142–148. With 1 map, 3 charts & 4 plates.

The high plateau of the Nilgiris in Southern India has been an endemic area of plague ever since its first occurrence early in 1903. Plague, however, has been declining steadily in the area. In this district potato farming has become a major industry and as field rats abound in potato farms, Government ordered an enquiry into the question of discouragement, by municipalities, of potato farming round the more residential areas. One purpose of the enquiry was to find out whether sylvatic plague, or factors favourable to its onset, existed. Out of 1,019 rodents and 1,939 fleas collected, plague infection was noted in only 3 rodents and 120 fleas. The plague rodents were *R. rattus* from a definite plague area. Typical rodents of the Nilgiris may be said to be *R. rattus*, *B. malabaricus* and *Gunomys kok*, representing respectively the domestic, semi-domestic and field species. In the case of Gunomys it was found that the predominating flea was *Stivalius* in Conoor and *Ceratophyllus* [*Nosopsyllus*] in Ootacamund. Plague transmission experiments were carried out with these two fleas, using white mice as the test animals, and it was found that *Stivalius* fleas " can transmit plague at least up to 3 days after feeding on an infected host." " It may also be reasonably concluded that *Ceratophyllus nilgirensis* is at least a weak vector of plague among rodents inasmuch as they retained live plague bacilli in their stomachs for over a week." No proof was forthcoming of the acutal existence of sylvatic plague in the district, but the enquiry, which is only taken to be preliminary, is not considered to have been on an adequate scale for the settlement of this point. *W. F. H.*

Central Provinces & Berar. Annual Report of the Public Health Department for the Year 1939 [Makand (S. N.), Director of Public Health]. pp. 17–19. With 1 chart.—**Plague.**

Plague was prevalent in some districts in epidemic form throughout the year, in others only for certain months and again in others sporadically or by reappearance after many years' absence. A graph of plague by months for the whole of the Central Provinces and Berar shows a maximum in March, with 210 deaths, and a fall to zero for June and July. The preventive measures employed were : evacuation, inoculation, disinsectization and rat destruction. Cyanogas A was used in certain municipal towns. *W. F. H.*

DAVIS (D. H. S.). **Some Ecological Methods in Research on Bubonic Plague.**—*South African Jl. Sci.* 1939. Vol. 36. pp. 438–444. [Summarized in *Rev. Applied Entom.* Ser. B. 1941. Apr. Vol. 29. Pt. 4. pp. 66–67.]

" Plague is now enzootic in the rodent population over a large area of southern Africa, and cases in man, reflecting the minimum extent of this area, have occurred during the last 20 years in parts of eastern and north-western Cape Province, the Orange Free State and borders of Basutoland, the southern and western Transvaal, Bechuanaland, South-West Africa and Angola. Sporadic cases occur annually in widely separated parts of the Union, mostly when the veldt rodent population has reached a peak and is being reduced by epizootics of plague. Until recently, the main source of infection in man has been *Mastomys coucha*, but lately *Mus* (*Rattus*) *rattus* has been the source, particularly in the Orange Free State, and on some occasions, large numbers of this rat have died without any traceable infection in the veldt rodents. It thus appears that *Mastomys coucha* and *Mus rattus* are forming reservoirs independent of gerbilles.

" Intensive ecological investigations were begun in September 1938 in an endemic plague area at Holfontein in the northern Orange Free State, with a view to devising quantitative methods of collecting data and of observing rodents and fleas in the field, and to using the results of intensive work in this small area as a standard for comparison with conditions in other parts of the country. An outline is given of the methods used to estimate the fluctuation of population among gerbilles (*Tatera brantsi*), which is of importance for the determination of the exact point in the population's growth at which epizootics of plague and other diseases break out. The bases of the study are observations in the warrens, which are described, marking experiments, and field observations and experiments on the reproduction of gerbilles. The chief fleas on *T. brantsi* in this area are *Dinopsyllus ellobius ellobius*, Roths., *Xenopsylla eridos*, Roths., and *Chiastopsylla rossi*, Wtstn., and the chief species on *M. rattus* is *X. brasiliensis*, Baker. *D. ellobius* and *X. eridos* were occasionally taken on rats and *X. brasiliensis* on *T. brantsi*. As flea numbers are controlled mainly by climatic conditions, a fluctuation in the population is brought about by seasonal changes in the burrows and places where the fleas breed, and owing to the different characteristics of the various species, there is also a fluctuation in their relative abundance. In plague investigations, the degree of parasitism by fleas is usually expressed as the average number of fleas per rat examined (flea-index). This, however, gives no indication of the flea population of the habitat of the host. By collecting all the fleas living in each burrow system of a warren, the total number could be ascertained and related to the gerbilles inhabiting the warren, and if the relation was shown to be constant, the flea-index would provide an estimate of the whole population. To collect the fleas, the entrances of all burrows appearing to form part of one system are marked, and the loose soil lying at the bottom of each burrow for one foot from the entrance is removed and kept in a numbered bag. The first foot is then dug away and a second sample taken, and this procedure is repeated until the whole system has been excavated. The position from which each sample is taken is marked on a plan as the work proceeds. The samples are then sifted and the fleas collected, and the dust is kept to allow any eggs, larvae or pupae

to develop. A description is given of an underground chamber where climatic conditions closely resemble those in gerbille burrows as indicated by records taken in an artificial burrow, which is also described; fleas can thus be studied in it in their natural climatic environment."

Congo Belge: Rapport sur l'Hygiène Publique au Congo Belge pendant l'Année 1939 [van Hoof (L.)].—[**Plague** pp. 14–15.]

The two foci of sylvatic plague in the east of the Colony were active in 1939; that near Lake Albert produced 65 human cases, of which 20 were septicaemic and 30 pulmonary. There was one case of primary plague meningitis. Prophylactic measures include rat destruction and the increasing use of the living E.V. strain for vaccination; in 1939, 8,871 natives were vaccinated without accident.

Two of the patients with pulmonary plague recovered after treatment with the sulphonamide preparation Astreptine, but 10 others so treated died.

Rattus rattus is absent from this focus; the rats concerned are of the genera Leggada, Arvicanthus, Lophuromys, Otomys, Lemniscomys, Pelomys and Mastomys. The fleas are Xenopsylla, Dinopsyllus and Ctenophthalmus.

In the focus of Lake Edward there was a small epizootic and two native children were infected, one of whom recovered after treatment with sulphanilamide. In this area *R. rattus* is found, and 90 per cent. of the fleas are *X. brasiliensis*. *C. W.*

Public Health Reports. 1941. Feb. 28. Vol. 56. No. 9. pp. 399–400.—**Plague Infection reported in the United States during 1940.**

During 1940 one case of human bubonic plague was reported in the United States. The patient was a boy of 13 living in Idaho, and the locality is close to the eastern counties of Oregon, which are known to be infected with rodent plague. The patient had been in contact with rabbits and carnivorous birds shortly before the onset of his illness. Details of plague in rodents and their parasites are given from five western States, California, Nevada, Oregon, Washington and Wyoming.

C. W.

Ackert (J. E.), Boles (H. P.) & Grundmann (A. W.). **Oriental Rat Flea established in Kansas.**—*Science.* 1941. June 13. Vol. 93, No. 2424. pp. 566–567.

Xenopsylla cheopis was found on specimens of *Rattus norvegicus* in Kansas in September 1940, and again, at Manhattan, Kansas, in April 1941. This indicates that the flea can overwinter there, and is established. The flea has been present in coastal cities since 1900, but has recently been reported from Indiana, Iowa, Minnesota, Illinois, Ohio and Tennessee. Its presence in Kansas, together with the eastward spread of sylvatic plague, make it evident that steps for control should be undertaken. Ground squirrels, mice and cottontail rabbits may harbour *X. cheopis*, but the principal hosts are rats. The field rodents, being susceptible to plague, are a potential menace to rats and measures against the latter are therefore necessary. *C. W.*

MACCHIAVELLO (Atilio). Investigaciones sobre peste en el nordeste brasileño. [**Plague in North-East Brazil.**]—*Bol. Oficina Sanitaria Panamericana.* 1941. May. Vol. 20. No. 5. pp. 441–462. English summary pp. 463–466.

These investigations were conducted by Brazilian specialists in collaboration with the Pan-American Sanitary Bureau and lasted from August 1939 to September 1940. They refer chiefly to rural areas, for urban plague has tended to disappear in recent years. It was thought possible that a form of sylvatic plague might exist, especially among preás (Brazilian opossums) and mocós (rock cavies). The conclusion was arrived at, however, that plague was really only epizootic among rats, especially *R. rattus*, and that its occurrence in other rodents was accidental and secondary. Some interesting facts were discovered during the investigations, which help to explain puzzling phenomena observed in the rural plague of north-east Brazil. The high temperatures prevailing at certain times of the year are unfavourable to transmission of plague by *X. cheopis*, which, however, finds more equable temperature in the nests of its rat host. At this time of the year, therefore, only a subterranean epizootic can occur and it is slow in its progress. With the advent of the rains the temperature drops, the fleas emerge from their shelters and plague makes its appearance above ground. Human cases occur and the disease " may even spread to wild rodents, possibly through the intermediation of *Monodelphis*[*sic*] *domesticus* and certain field mice." Another factor to which importance is attached is the occurrence of non-plague epizootics among various wild animals. If human plague coexisted with these other diseases, it may have been too hastily assumed that sylvatic plague was present in Brazil. The organisms causing these non-plague epizootics seem to have been largely of the Pasteurella class—*lepiseptica, pseudotuberculosis rodentium, avicida, muricida* and some organisms of other genera.

No evidence of chronic plague could be found and some of the re-introduction of plague into areas from which it had disappeared may have been due to migration of rodents. A disease known locally as *ingua de frío* (cold bubo) or *febre de caroço* (stone fever) was proved for the first time bacteriologically to be truly plague. The name of " stone " applied to the disease represents the tendency of the bubo " to become ligneous." It has " a propensity for recurrence or to be reabsorbed." A new plague syndrome was also noted, describable as multiglandular fever, in which localized suppuration, gastro-intestinal and urinary symptoms, septicaemic fever and wasting were prominent and in which the mortality was low. What is regarded as the first human case on record of mixed infection by *P. pestis* and *P. pseudotuberculosis rodentium* is described. *W. F. H.*

D'AMATO (Hugo J.). Focos de peste en el centro y norte de la republica. [**Plague Foci in the Centre and North of the Argentine.**] —*Bol. Sanitario.* Buenos Aires. 1940. Sept.–Dec. Vol. 4. Nos. 9, 10, 11 & 12. pp. 606–608.

In this broadcast talk the author refers to recent outbreaks: in the Province of Salta, Anta, Cerrillos, Rosario de la Frontera and Metán ; in the Province of Santiago del Estero, Pellegrini and Giménez ; in Tucumán, Burruyacú, Graneros and Cruz Alta. All the cases in

these places were of the bubonic type. In Jujuy, at Ledesma, in Córdoba, at Totoral and San Javier there were pneumonic cases, and in San Luis, Santa Rosa, septicaemic plague has been seen.

The remainder of the talk is concerned with the importance of the anti-rat campaign and the construction of an impermeable barrier against field rodents round the centres of population. *C. W.*

Pardal (Eduardo). Informe sobre el caso de peste ganglionar registrado en el lugar denominado Colonia Fraga, 10 kilometros al sudoeste de la Estación Fraga, F.C.P., Departamento Pedernera de la provincia de San Luis. [**Report on a Case of Plague.**]—*Bol. Sanitario.* Buenos Aires. 1940. Sept.–Dec. Vol. 4. Nos. 9, 10, 11 & 12. pp. 609–614.

The case of plague reported was registered as originating in a place called Colonia Fraga. This place had never had any case of plague and the account given of the patient was that he had been catching armadillos for food a few days before he fell ill. No evidence of the existençe of *Mus rattus* in this place was forthcoming, but there was an abundance of moles, vizcachas and armadillos. The inhabitants of the place did not think that rodents such as cuis or Graomys were to be found. However, when special search was instituted with the help of a greyhound the catch made was of two armadillos, two Graomys and a cui. An accident happened to this material and it was only possible to examine bone marrow of the cui and Graomys. Armadillos are not susceptible to plague. The bone marrow of the cui alone furnished plague colonies proven to be plague by inoculation in guineapigs. Fleas obtained from the armadillo gave no positive result. It is thought by the author that the patient must have contracted his plague from infected plague fleas, derived from some infected rodent, and carried by the armadillos, although he does not by any means exclude the possibility of a direct infection by fleas. This explanation would make this case of plague sylvatic in its origin.

W. F. H.

Moll (Arístides A.) & O'Leary (Shirley Baughman). **Plague in the Americas: an Historical and Quasi-Epidemiological Survey.**—*Bol. Oficina Sanitaria Panamericana.* 1941. Feb. Vol. 20. No. 2. pp. 139–149. With 1 map. [Refs. in footnotes.]

[The number containing part IV of this series has not been received.]

V. *Chile.*—In Chile plague has been restricted almost entirely to ports " and especially those of the northern, desert, saltpeter area." The first case actually diagnosed occurred in Iquique in 1903 and was followed by an outbreak which lasted for about four months with 214 confirmed cases and a 63 per cent. mortality. Epidemics have occurred mainly in summer and autumn when the area extending from the northern boundary to Valparaiso is favourable to flea activity. " The climate south of Valparaiso seems to be unfavourable to *X. cheopis* ; and in the northern area the ports are surrounded by the dry desert-like Pampa, with a temperature varying perhaps 50° in a single day and night ; with few rats and no fleas so that plague did not spread to the interior." No human plague has been reported since 1931 and no rat plague since 1932. *W. F. H.*

HAWAII, TERRITORY OF: BOARD OF HEALTH. REPORT FOR FISCAL YEAR 1940 [HARALSON (M. F.)]. pp. 79–81.—**Plague Control.**

In the Territory of Hawaii plague seems to have disappeared completely from the island of Oahu as no case of plague has occurred there since 1910. On Mani neither human nor rodent plague has been found since December 1937, but the antiplague campaign is still vigorously carried on as a preventive measure. Hawaii itself is still a centre for plague. In one area 47 cases of rodent plague and one case of human plague were discovered during the year. Rat eradication by trapping and poisoning with banana-phosphorus bait have been the chief plague measures employed.

Plague is not at present a problem on any of the islands, other than those mentioned. *W. F. H.*

KAMAL (Ahmed Mohamed). **On the Epidemiology of Plague in Assiut Province in the Years 1938–1939.**—*Jl. Egyptian Public Health Assoc.* 1941. Jan. 16th Year. Spec. No. pp. 1–30.

Plague is endemic in Egypt and cases of the disease occur nearly every year. This account of the epidemiology of plague deals with the particular towns and villages of the country. Excerpts of observations on some of these have decided interest. In the village of Awlad Elias 4 cases occurred in February and the whole village was vaccinated by the 9th March. In spite of this, however, a new case was reported on 14th March, followed by others, making a total of 23 in April, with another 6 in May. Another interesting observation made is regarding the possibility of mild plague. In one epidemic for example "it was customary to meet a large number of children with an enlarged gland or 'bubo,' sometimes tender sometimes painless" but with no other symptoms. In the author's opinion most, if not all such cases are "inapparent" or "ambulatory" plague. He deals specifically with the effect of vaccination, but regards as vaccinated only those who had received two doses or in whom the three weeks considered necessary for establishment of immunity had elapsed. With this limitation in the numbers of the truly vaccinated a mortality of 34·3 per cent. was found among the non-vaccinated and 25 per cent. among the vaccinated plague cases of Abu Tig district. Actual cases of plague were treated with serum in doses, for the adult, of 20 and 30 cc. per day, doses which were pushed higher still to as much as 50 cc. and sometimes 80 cc. The results with big doses of serum are considered to be on the whole gratifying. *W. F. H.*

KAMAL (Ahmed Mohamed), GAYED (Ishac) & ANWAR (Mohd.). **On the Epidemiology and Treatment of Plague in Egypt. "The 1940 Epidemic."**—*Jl. Egyptian Public Health Assoc.* 1941. Jan. 16th Year. Spec. No. pp. 31–103. With 8 maps, 2 graphs, 3 figs. & 41 charts.

Plague history of recent times in Egypt begins in 1899 when the disease reached Alexandria. From that date it has appeared yearly. During 1940, Assiut Province was visited by a severe epidemic which was reported from five administrative districts. A very large proportion of the population of the epidemic areas seems to have been inoculated, 70,588 persons out of 84,518, and this with double the dose

used in previous years, namely 1,000 million bacilli for the first dose and 2,000 million for the second. The authors recognize the necessity for putting any prophylactic vaccine method to an alternate case control. For this particular test they chose 19 villages and inoculated half families throughout, 15,801 persons out of a population of 41,085 inhabitants. Unfortunately this interesting and important trial failed, because plague did not attack the localities chosen. Their opinion, however, of vaccination does not seem to be very high, for they " are convinced that vaccination en masse and during epidemics neither reduces the chance of acquiring the disease nor stops the epidemic." They think that the fatality of bubonic plague is decidedly lower among the vaccinated than the non-vaccinated.

One of the features peculiar to the epidemiology of plague in Egypt is its relation to the presence of pigeon houses put up by the inhabitants. The excreta of the pigeons is used for manure : these houses are badly infested by rats and it is this which makes of them a real plague danger.

Among the interesting observations on the symptomatology of plague is the mention of tonsillar bubo, plague meningitis and plague pyomyositis. A combined treatment of plague with serum and Dagenan [sulphapyridine] appears to have been superior to other forms of treatment. *W. F. H.*

Murdock (John R.). **Pneumonic Plague in Ecuador during 1939.**—*Public Health Rep.* 1940. Nov. 22. Vol. 55. No. 47. pp. 2172–2178.

The history of the three outbreaks of plague here described is interesting because of its significance for the occurrence of secondary pneumonia developing in the first instance on ordinary bubonic plague. Diagnosis may not be made immediately and the danger of transmission applies not only to friends and relatives of the patient but also to doctors and nursing sisters. These are features which are illustrated in all three Ecuador epidemics. A fairly common group of symptoms characterizes the illness :—chills followed by headache, fever, generalized pains and prostration to begin with. After 24 hours appears a soft easy cough with little expectoration, which is mucoid and becomes flecked with pus and then blood. The sputum is adhesive and stringy : on microscopic examination it is found in most cases to show plague bacilli almost exclusively.

In the author's opinion outbreaks of pneumonic plague are almost always due to a case of bubonic plague which has developed secondary pneumonia but it is " not always possible to establish the connection between the first pneumonic infection and the bubonic cases that produced it." Active steps should be taken as soon as the pneumonia is diagnosed to quell the outbreak. The best methods are :—" (1) To isolate rigidly the infected patients . . . . (2) To quarantine all persons who have been in direct contact with the infected person . . . . (3) To protect nurses and doctors in attendance by suitable head masks, gowns and rubber gloves. (4) The careful disinfection and fumigation of quarters previously occupied by pneumonic plague patients. (5) House-to-house inspection of persons in infected sectors, with temperature taken twice daily and isolation of all who show temperature regardless of cause." *W. F. H.*

Junior (Marcello Silva) & de Albuquerque (Rodrigues). Reacção allergica do mal de Yersin. Nota prévia. [**An Allergic Reaction in Plague.**]—*Brasil-Medico.* 1940. Nov. 16. Vol. 54. No. 46. p. 759.

The authors have made use successfully of an intradermal allergic reaction for diagnosis in cases of suspected plague. To obtain the necessary antigen they inoculated a guineapig with a recent culture of plague, removed a regional lymph node immediately after the death of the animal, boiled the node for two hours in normal salt solution, ground it up in a mortar to obtain a suspension, and filtered through sterile gauze. A dose of 0·1 cc. of the suspension was used for intradermal injection. Ten out of 12 individuals tested gave a positive reaction which was at a maximum after 36 hours. The reaction consisted of a central papule surrounded by an inflammatory zone. There was good reason to think from the clinical symptoms that the two individuals with negative reaction were not suffering from plague. It seems likely that the reaction may also prove useful retrospectively to confirm a diagnosis of probable plague which should help to make epidemiological statistics more exact. *W. F. H.*

Wagle (P. M.), Sokhey (S. S.), Dikshit (B. B.) & Ganapathy (K.). **Chemotherapy in Plague.**—*Indian Med. Gaz.* 1941. Jan. Vol. 76. No. 1. pp. 29–32.

The important and well controlled trials here recorded on 237 cases of bubonic plague, which had been bacteriologically verified, represented four different methods of treatment :—antiplague serum, sulphapyridine (M. & B. 693), sulphathiazole, and the routine treatment of iodine solution intravenously. All the cases were taken strictly in serial order and no difference was made between septicaemic and non-septicaemic cases.

Taken in the above-given order the numbers of cases treated were 70, 53, 32 and 82, with case mortalities of 28·5, 24·5, 15·6 and 52·4 per cent. respectively. As the authors point out, upwards of 50 per cent. died of the infection when treated with iodine, which means that " the serum, sulphapyridine and sulphathiazole treatments produced a significant reduction in the case mortality." Statistically, however, there does not appear to be any significant difference between the results with serum, sulphapyridine and sulphathiazole. When only the plague septicaemia cases are considered the serum case mortality worked out at 60·6 per cent. as compared with sulphapyridine and sulphathiazole with 43·3 and 41·8 per cent. respectively, while the iodine controls showed a mortality of 95 per cent. It is probable, from these trials, that serum cannot be given in sufficient dose intravenously because of the alarming symptoms of serum shock which are liable to develop. Six patients suffering from primary pneumonic plague were also treated, two with iodine and four with sulphathiazole. All these died and " the characteristic feature of the cases treated with sulphathiazole was that daily cultures from the blood remained sterile " whereas in the iodine cases " plague bacilli appeared in blood about 24 hours after admission." *W. F. H.*

Chopra (R. N.), deMonte (A. J. H.) & Chatterji (B. C.). **A Case of Plague Successfully Treated with Sulphapyridine.**—*Indian Med. Gaz.* 1941. Feb. Vol. 76. No. 2. pp. 89–90.

This case is noteworthy not only for a successful termination by recovery, but also for the intensive treatment adopted and for the absence of all signs of intolerance. The patient, a female, rather ill-nourished, child aged six years, had developed a bubo and fever one day before admission to hospital. Plague bacilli were isolated from the bubo before treatment commenced. Treatment consisted in the administration of sulphapyridine by mouth and the soluble sodium derivative of sulphapyridine in gramme doses daily by intramuscular injection. The lung condition progressed to bronchopneumonia before improvement set in. Altogether the child " received 31·5 gm. of sulphapyridine of which 29·5 gm. had been administered during the first eight days of the stay in hospital." It was found that *P. pestis* could be isolated from the bubo before administration of sulphapyridine, again 12 hours later after 1·5 gm. had been given orally, but not from samples subsequent to the administration of 14 and 20 gm. of the drug.

W. F. H.

Journal of the Egyptian Public Health Association. 1941. Jan. 16th Year. Spec. No. pp. 131–146. With 1 plan & 19 figs. —**Appendix I. Résumé of the Routine Antiplague Measures adopted in Egypt. Appendix II. Data of Plague Investigation.**

In villages a death rate of three per thousand is considered normal and no steps are taken with regard to deaths. " If the mortality in the village exceeds that limit, or if more than one death occur in the same family within six weeks " the body is kept for the M.O.H., who may permit burial. If, however, an acute disease is suspected, punctures are made of heart, liver and lungs, and the material obtained is sent for examination to the district bacteriologist. At the same time disinfection of house and contacts is carried out and the contacts are all examined for infectious disease. Once plague is reported in any locality measures are taken for the admission of patients to hospital and for the isolation of contacts, especially the contacts of pneumonic or septicaemic cases. Disinfection and disinfestation of houses is also an important part of the routine plague practice. *W. F. H.*

Hopkins (G. H. E.). **Methods of Control of Plague in Uganda.**—*East African Med. Jl.* 1941. Apr. Vol. 18. No. 1. pp. 18–24.

Prophylactic inoculation and the quarantining of plague cases are the measures of control applied to man. Only persons who have been specially exposed to risk of infection are inoculated. The main control measures are those applied to rats and fleas. Rat proofing of stores, removal of harbourage for rats and the maintenance of a cleared zone round buildings are legislated for. Unfortunately this does not always mean that the regulations are strictly carried out. Fumigation of huts with Cyanogas is extensively employed, and investigation shows that roughly a quarter of the rat population survives the gassing. This is not considered satisfactory, especially as fleas are killed less rapidly than the rats. It is advisable in the gassing of huts to remove the thatch and owners will not object to this so much if they are allowed

to use the thatch again. A useful precaution in these gassing operations is the provision of at least one gas mask. Apart from danger to the operating staff there is always the possibility that livestock, bolting into the hut, may have to be rescued after gassing has begun.

W. F. H.

MEYER (K. F.). **Sylvatic Plague.**—*Amer. Public Health Assoc. Year Book 1940–1941* (*Supp. Amer. Jl. Public Health.* 1941. Mar. Vol. 31. No. 3.) pp. 145–148.

TRYPANOSOMIASIS.

Précis OF ABSTRACTS IN THIS SECTION.

WALKER (p. 631) states that the 20,054 cases of sleeping sickness discovered in Nigeria during 1939 represent an average incidence of 4 per cent. of the natives examined, but that in the Benue province the rate reaches 6·7 per cent. In the miners of the Kabba-Ilorin goldfield the incidence is as high as 40 per cent. He gives information on the progress of control measures. VAN HOOF (p. 631) reports on sleeping sickness in the Belgian Congo during 1939, when 12,886 new cases were discovered and 40,510 were under control.

JACKSON (p. 632) reports further work on the study of marked *Glossina morsitans* observed in natural surroundings in Tanganyika Territory.

VANDERPLANK (p. 632) records experiments which indicate that the transmissibility to *Glossina morsitans*, and the virulence to the rat, of a strain of *Trypanosoma rhodesiense*, may be enhanced by passage through animals with low mean body temperatures. HAWKING (p. 633) examined strains of *T. rhodesiense* from untreated patients and from patients who had relapsed after treatment with tryparsamide, and found that the latter were more resistant to tryparsamide than the former. It seems probable that this is an acquired resistance and is not due to previously resistant trypanosomes persisting and causing the relapses.

FRIEDHEIM (p. 633) reports on the treatment of human sleeping sickness in West Africa with triazine arsinic acid. This drug can be given either intravenously or subcutaneously; details of dosage in early and in later cases are given. The therapeutic effect in early cases was rapid sterilization of the blood and gland juice even after oral administration; in second stage patients there was reduction of cells and albumin in the cerebrospinal fluid, with clinical improvement. The period of observation of the 86 patients in whom the treatment was pursued was comparatively short, but the results so far are good.

STEWART (p. 636) points out that in the Gold Coast the block method of clearing is insufficient to meet the needs of the Veterinary Department, though it is favoured by medical entomologists.

WOTTON (p. 636) has made a study of the mitochondria seen in certain species of trypanosomes.

Chagas's disease.—PACKCHANIAN (p. 637) has succeeded, by the injection of suspensions of *T. cruzi* into rabbits, in producing serum which will agglutinate *T. cruzi* in high titre.

Pereira (p. 638) describes a method of collection of faeces of Reduviid bugs for examination or for animal inoculation. Martins (p. 639) has shown that the new species *Triatoma arthurneivai* is capable of becoming infected with *T. cruzi*.

Dias (p. 639) shows that cats and dogs which eat rodents infected with *T. cruzi* may themselves become infected, and states that they may also acquire infection by eating infected insects.

Pifano and Dias (p. 639) in Brazil found bats infected with a trypanosome which could infect Reduviid bugs, *Cimex hemipterus* and *Ornithodorus moubata* and which could be cultivated and used to infect laboratory animals. Work is in progress to determine if this trypanosome is *T. cruzi*.

Martins and Tupynamba (p. 639) give an account of two patients with Chagas's disease who presented Romaña's sign.

Mayer and Pifano (p. 640) have prepared from *T. cruzi* an antigen which they name cruzin and which, when injected intradermally, is apparently of great value as a rapid diagnostic agent. *C. W.*

Nigeria. Report on the Medical Services for the Year 1939. Appendix B. pp. 15–16.—**Report of the Sleeping Sickness Service, 1939** [Walker (G. B.), Acting Director of Medical Services].

During 1939, 494,428 people were examined by the Sleeping Sickness teams, and 20,054 cases were found, an average of 4·0 per cent., chiefly in the Benue Province, where little work had been done before 1938, and where the incidence was as high as 6·7 per cent. In all 30,090 cases were given treatment. In the Zaria Emirate where mass campaigns have been functioning since 1933, the total population has increased greatly, and sleeping sickness is now only a fraction of what it once was. There is a high incidence of a virulent type of disease in the miners of the Kabba-Ilorin gold field, where the rate is as high as 40 per cent., and it is thought that it was brought into the district by labourers from further north.

The settlement schemes have made good progress, and most of the preliminary work on the fly-free corridor of 680 square miles has been done. Limited clearing only will be necessary to free the northern parts from tsetse, and movement of villages on a big scale will not be required. Most of the tributary streams dry up in the dry season, and barrier clearings are being made to prevent tsetse from spreading back during the rains from the permanent foci on the main rivers.

More than half the corridor has now been freed from tsetse, and land for new settlements has been chosen carefully with a view to agricultural and pastoral development.

The war interfered with sleeping sickness work and the number of teams was reduced to three, but the dispensary system is being expanded to compensate for the reduction in mass treatment.

C. W.

Congo Belge : Rapport sur l'Hygiène Publique au Congo Belge pendant l'Année 1939 [van Hoof (L.)].—[**Trypanosomiasis** pp. 25–39. With 1 folding map.]

Ten European cases of sleeping sickness were treated during the year : 6 of these in the province of Léopoldville, 1 in Lusambo, 2 in Coquilhatville and 1 in Elisabethville. During 1939, all the

endemic areas were visited by the medical service. The total number of natives visited exceeded 5 millions. The number of old cases kept under control was 40,510, and the number of new cases discovered 12,886. In a table, information is given regarding the number of cases examined, old cases controlled, new cases discovered and the index of new infection during each of the years 1927–1939. In other tables, the distribution of the disease in the various provinces is recorded.

The paper is illustrated by an excellent map showing the endemicity of sleeping sickness in the various parts of the Belgian Congo in 1939.

W. Yorke.

JACKSON (C. H. N.). **The Economy of a Tsetse Population.**—*Bull. Entom. Res.* 1941. Apr. Vol. 32. Pt. 1. pp. 53–55.

This paper records work in continuation of that reported in this *Bulletin*, 1941, Vol. 38, p. 74 ; all the results were obtained from marked *Glossina morsitans* at Kakoma, Tabora, Tanganyika Territory. The life of the flies is shortest in the hot dry season when death is probably due to failure to meet food. In this season males may live for only two weeks, whereas in the rains they survive five to six weeks as a rule, some fortunate individuals living as long as 20 weeks. At all seasons females live possibly twice as long as males ; the female population is therefore perhaps twice as great as the male. The birth rate agrees fairly closely with the death rate and there appears to be little seasonal variation.

Flies live in somewhat restricted ambits, in which they move freely, and which are determined by the disposition of the vegetation. There is a relatively slow rate of drift outside the ambit and it follows that wandering game animals have very little effect in aiding the dispersal of flies. Probably the average distance travelled by a male fly in either direction from a given straight line does not greatly exceed half a mile during its whole life, but the female ambits are rather larger.

Revised estimates show that there are about 1,000 males per square mile, and perhaps twice as many females. If the seasonal firing of bush is excluded, the fly population has been observed to fall until the middle of the rains, after which it rose to equal that in the control area. This fall may be due to destruction of pupae by ants (Pheidole).

The length of life of marked flies is less than that of unmarked, but the reason for this is not apparent. *C. W.*

VANDERPLANK (F. L.). **A Note on the Relation between the Virulence of *Trypanosoma rhodesiense* towards Rats and the Normal Blood Temperature of its Previous Mammalian Host.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1941. July 3. Vol. 35. No. 1. pp. 43–46.

Experiments are recorded which suggest that the transmissibility to the fly, and the virulence of a strain of *T. rhodesiense* in rats, may be enhanced by passing it through animals with a low mean body temperature.

The work was undertaken at the Human Trypanosomiasis Research Station, Tinde, after the retirement of Dr. Corson. The history of the *T. rhodesiense* strain used in the experiments has been published by CORSON [this *Bulletin*, 1939, Vol. 36, p. 662]. Various antelopes and other animals infected with this strain were kept at Tinde and the strain was transmitted by *G. morsitans*. In order to isolate the infected

flies, they were fed singly on numbered rats, which were examined for trypanosomiasis daily for a fortnight. Young healthy adult male rats were used during these isolations.

The observations are summarized in two tables. Table I gives the length of life in days of rats which were infected by *G. morsitans* transmitting *T. rhodesiense* from sheep, goat, monkey, eland, reedbuck, impalla, dik-dik, and Thomson's gazelle, respectively. The mean length of life of the rats bitten by *G. morsitans* infected from these various sources ranged from 66·8 days in the case of the sheep to 30·5 days in the case of Thomson's gazelle.

Table II gives the number of infected animals of each sort used to infect flies, the rectal temperatures before the animals were infected, the number of animals used to obtain mean temperatures, the percentage of original flies infected, and other data. It is seen that the rectal temperature varied from 103·4°F. in the case of the sheep to 98·7°F. in Thomson's gazelle, and the percentage of flies infected varied from 1·5 in the case of the sheep to 9·6 in that of Thomson's gazelle.

W. Y.

HAWKING (Frank). **Drug Resistance acquired during the Treatment of Sleeping-Sickness with Tryparsamide and with Bayer 205.**—*Amer. Jl. Trop. Med.* 1941. May. Vol. 21. No. 3. pp. 469–479.

The object of the work described in this paper was to ascertain to what extent trypanosomes become resistant during the treatment of infected human beings. The sensitivity to tryparsamide of strains of *T. rhodesiense* freshly isolated from untreated cases of sleeping sickness is compared with that of similar strains isolated from patients who relapsed after one or more courses of treatment with this drug. The work was carried out during 1938 at Kahama, Tanganyika Territory.

The technique adopted consisted in infecting rats with the trypanosomes from the various patients. From rats of the first passage, other rats were inoculated intraperitoneally. After about five days, when the blood contained about 1–20 trypanosomes in each high power microscope field, the rats were injected intraperitoneally with suitable doses of tryparsamide. The blood was examined for the next three days ; if no trypanosomes were seen in 30 fields, the blood was taken to be negative. The minimum effective dose was taken as the least dose sufficient to make the blood of the majority of the group negative on two of the first three days.

Strains were obtained from 23 untreated patients and from four patients who had relapsed after repeated injections with tryparsamide. In addition, the old laboratory strain of *T. rhodesiense* from Liverpool was also tested. Details are given in tables, from which it is seen that the trypanosomes from patients relapsing after treatment with tryparsamide have a greater resistance to this compound than have those from untreated patients. The resistance, however, is not so great as might have been expected from animal experiments. At Liverpool it was found by YORKE and his colleagues that when infected rabbits relapsed after tryparsamide, the resistance of the trypanosomes often became so great that they were no longer influenced by the maximum dose of drug tolerated by the mice used for the dose. [A probable explanation of this is the fact that the experimental rabbits of the reviewer and his colleagues had received a relatively much greater

dosage of tryparsamide than had Hawking's patients. Hawking does not state the size of the individual doses his patients received, but presumably they were not more than 2 or 3 gm. per week for a 50-kilo. man; the doses given by Yorke and Murgatroyd were considerably greater.]

Hawking states that the greater resistance of trypanosomes from patients who have relapsed may be explained in two ways: it may be acquired resistance obtained during the unsuccessful treatment with tryparsamide, or it may be natural resistance, originally present and responsible for the relapse. Results of animal experiments suggest that the former is the correct explanation, and this is supported by one of Hawking's human cases, whose trypanosomes were tested both before and after the second course of tryparsamide; in this case it seems almost certain that a definite increase of resistance had occurred during this period.

The author made a few observations on patients who had relapsed after treatment with Bayer 205, but obtained no evidence that the trypanosomes from these patients exhibited an increase of resistance to this compound. *W. Y.*

FRIEDHEIM (Ernst A. H.). L'acide triazine-arsenique dans le traitement de la maladie du sommeil africaine. Etude expérimentale et clinique. [**Triazine Arsinic Acid in the Treatment of Sleeping Sickness.**]—*Schweiz. Med. Woch.* 1941. Feb. 1. Vol. 71. No. 5. pp. 116–119.

This paper gives the results of a clinical trial of an aromatic arsenical prepared by the author, *viz.*, 2 : 4-diamino-6-(arsono-anilino)-triazine. The di-sodium salt of this substance, which for the sake of brevity has been called triazine arsinic acid (No. 4289) is a white crystalline powder containing 20·2 per cent. of arsenic and is soluble in water to the extent of a 33 per cent. solution. In the dry form it is stable and does not change when kept for four months at a temperature of 65°C. The solution is stable during a period of three months at 45°C.

In preliminary biological observations, the author examined the toxicity of the substance for mice. It was found that doses of 0·75 and 1·0 gm. per kilo., given intravenously, killed respectively 10 per cent. and 20 per cent. of the animals. When the drug was given by the mouth, mice stood 10 gm. per kilo, without any inconvenience. Rabbits tolerated a dose of 0·75 gm. per kilo. intravenously and dogs about 0·2 gm. per kilo. In the following table the author compares the trypanocidal action of his new compound, *viz.*, No. 4289, with that of tryparsamide in *T. equiperdum* infections of mice:—

	Min. Cur. Dose gm./kgm.	Max. Tol. Dose gm./kgm.	Therapeutic Index
Tryparsamide intraperitoneally	0·4	2·25	5·6
4289 intraperitoneally... ...	0·03–0·05	1·5	*circa* 30

From this it appears that the new substance is about eight times more active than tryparsamide, and that its therapeutic index is

considerably greater. Experimental intoxication does not produce the phenomenon of waltzing mice, *i.e.*, signs of nervous lesions, as is the case with tryparsamide. The maximum tolerated dose varies with the volume of liquid injected and with the quantity of water absorbed by the mouse after the injection.

In 1939, the author had an opportunity of visiting French West Africa and of testing his substance on 89 cases of human trypanosomiasis. His work was divided into three stages, *viz.* (1) to establish under good hospital and laboratory conditions on a limited number of cases the trypanocidal effect and essential facts regarding the posology and pharmacology of the preparation; (2) to establish on a more considerable number of cases the facts obtained in his preliminary investigations, to study more particularly the effect of the preparation on the changes in the cerebrospinal fluid, and finally to establish a standard routine of treatment applicable to conditions in the bush; (3) to examine all the patients treated, six months to a year after the end of treatment.

The first part of this programme was carried out in the neighbourhood of Dakar and the second part in the interior of the Ivory Coast, at the trypanosomiasis school of Ouagadougou. The third part has been prevented by the outbreak of war.

The drug can be given either intravenously or subcutaneously with practically the same results. For patients in the first stage of the disease, the author recommends doses of 0·03 gm. to 0·5 gm. per kilo. with a maximum of 2 gm., every third day. The course of treatment consists of 10 injections during a period of about 30 days. It is important to commence treatment in second stage cases, exhibiting signs of meningo-encephalitis, with small doses given subcutaneously. In such cases a first dose of 0·03 gm. per kilo., which is perfectly tolerated by first stage cases, may be followed by a severe reaction with an aggravation of all the encephalitic symptoms. This veritable crisis is analogous with a Herxheimer reaction. A week later, when it has passed, the patient will be able to tolerate the usual course of treatment without inconvenience.

The author recommends the following plan of treatment in second stage cases: first subcutaneous injection 0·01 gm. per kilo., second subcutaneous injection 0·02 gm. per kilo., third subcutaneous injection 0·03 gm. per kilo., fourth injection, which can be given either subcutaneously or intravenously, 0·03 gm. per kilo., and the fifth and following injections, either subcutaneous or intravenous, 0·03–0·04 gm. per kilo. Eleven patients in whom the cerebrospinal fluid contained 87–946 cells per cmm. and eight cases with trypanosomes have been treated in this way without any inconvenience or accident.

The only toxic effects observed after large doses of the drug were gastro-intestinal disturbance, *i.e.* vomiting, colic, diarrhoea, and arsenical dermatitis; these disappeared quickly when the drug was stopped. Albuminuria and disturbance of vision were never seen.

Therapeutic effects.—All the 76 cases treated parenterally with the compound became negative after the first injection. In 32 of them peripheral sterilization was observed 24 hours after the first injection. Twenty-nine cases have been re-examined 2½ to 9 (mainly 6 or 7) weeks after the end of treatment; these examinations showed the patients to be clinically cured and free from parasites. The effect on the pathological changes in the cerebrospinal fluid exhibited by 19 second stage cases is shown in a table. The drug produced a rapid

diminution in the number of cells in the cerebrospinal fluid but the quantity of albumin diminished more slowly. The clinical signs and symptoms were also rapidly ameliorated. Somnolence and locomotory disturbances diminished towards the end of the second week, but such troubles as tremors and rigidity improved to a slight extent only.

Oral treatment.—Experiments on laboratory animals showed that mice tolerated remarkably large quantities of the drug when it was administered orally. For example, all of 20 mice tolerated 10 gm. per kilo., *i.e.* 0·2 gm. per mouse. The minimum curative dose by the oral route was also raised to 0·5 gm. per kilo. Thus, when the drug is given by this method the therapeutic index is about 20. In man, it was found that isolated doses of 0·12 gm. per kilo. and repeated doses of 0·09 gm. per kilo. every day for a week were perfectly tolerated. The general plan of treatment adopted was the daily ingestion during a period of two or three weeks of a dose of 0·07 to 0·1 gm. per kilo. This treatment was administered to 13 patients, of whom nine were in the first stage and four in the second stage of the disease. Ten patients tolerated the treatment without any inconvenience. In three cases the daily dose was tolerated up to the 10th, 12th and 13th day respectively, when gastro-intestinal symptoms began to manifest themselves, rendering necessary suspension of treatment for a few days. There was no renal or visual disturbance. The after-effect of oral administration was slower than when the drug was given parenterally, but the blood and gland juice were negative in all cases within three days. No relapses were observed. In the four second stage cases the number of cells and the quantity of albumin in the cerebrospinal fluid were considerably diminished. *W. Y.*

KIKUTH (Walter). Die afrikanische Schlafkrankheit und ihre Bekämpfung. [**African Sleeping Sickness and its Control.**]—*Deut. Med. Woch.* 1940. Dec. 6. Vol. 66. No. 49. pp. 1363–1366.

This is a general statement of the situation, containing nothing new. *C. W.*

GOLD COAST. REPORT ON THE DEPARTMENT OF ANIMAL HEALTH FOR THE FINANCIAL YEAR 1939–40 [STEWART (J. L.), Director of Veterinary Services]. pp. 3–4.—[**Trypanosomiasis.**]

It is noted that in 1939 there was a much higher incidence of trypanosomiasis in cattle than is usual. This was attributed to the irregular and excessive rainfall which produced much flooding, with the result that flies were driven further afield in the rains.

Clearings undertaken by the Veterinary Department are always entire; the block method, along rivers, favoured by medical entomologists is not enough in veterinary practice, since one aim is to eliminate wild carnivora and to lower the numbers of crocodiles in the rivers so that in the dry season herds of cattle can use the cleared valleys as dry season grazing grounds. Complete clearing allows a profuse growth of grass within the banks of the rivers, and this makes excellent dry season grazing. *C. W.*

WOTTON (Robert M.). **A Study of the Mitochondria of Trypanosomes.**—*Quarterly Jl. Microscopical Sci.* 1940. Oct. Vol. 82. Pt. 3. (N.S. No. 326). pp. 261–266. With 1 plate. [17 refs.]

It has long been recognized that granules of indeterminate character are to be seen in the cytoplasm of certain species of trypanosomes.

Shipley made a careful study of these granules in 1916, and concluded that they were mitochondria.

The present paper reports the results of the study of several species of trypanosomes with respect to the possible presence of mitochondria. The trypanosomes studied were: *Trypanosoma lewisi*, *T. duttoni*, *T. melophagium*, *T. cruzi* and *T. equiperdum*. The parasites were studied in films made from the blood of experimentally infected rats, mice and guineapigs, in preparations made from cultures of *T. cruzi* and from the insect vector (*Melophagus ovinus*) of *T. melophagium*. The staining technique employed is described in detail.

Mitochondria were demonstrated in the adult forms of the various trypanosomes found in the blood of the vertebrate hosts, and also in the crithidial forms of *T. cruzi* from culture and *T. melophagium* from the insect vector. No essential morphological variations in the mitochondria were observed among the five species of trypanosomes studied, or among the several growth stages.

The author considers that in view of the morphological similarity between the mitochondria of trypanosomes and the mitochondria found in higher species of animals, there is a great likelihood of a similarity in function. Notwithstanding the numerous studies of these cytoplasmic elements amongst cells of the higher forms, their specific nature and function remain obscure, but there is reason to believe that these elements are associated with metabolism. A similar metabolic activity may be implied for the mitochondria in trypanosomes, and as a result of the author's study on *T. lewisi*, it is suggested that this function is connected with fat metabolism. *W. Y.*

Wood (Fae D.) & Wood (Sherwin F.). **Present Knowledge of the Distribution of *Trypanosoma cruzi* in Reservoir Animals and Vectors.**—*Amer. Jl. Trop. Med.* 1941. Mar. Vol. 21. No. 2. pp. 335–345. [68 refs.]

Cardoso (Francisco A.). Epidemiologia e profilaxia da moléstia de Chagas. [**Epidemiology and Prophylaxis of Chagas's Disease.**]—Reprinted from *Rev. de Med.* São Paulo. 1940. Oct. Vol. 24. No. 82. pp. 49–75. [54 refs.]

Packchanian (Ardzroony). **Experimental Production of Agglutinins for *Trypanosoma cruzi*.**—*Public Health Rep.* 1940. Nov. 15. Vol. 55. No. 46. pp. 2116–2124. [11 refs.]

This paper gives a description of the technique of the microscopic agglutination test for the diagnosis of *T. cruzi* infection, and the results obtained by such procedure.

The preparation of the *T. cruzi* antigen for immunization and agglutination tests is described in detail. *T. cruzi* was grown from 1 to 3 weeks on rabbit blood agar slants at 25°C. The tubes were sealed either with rubber caps, rubber stoppers, or sealing wax. After about 10 days' cultivation the growth from the tubes was suspended in Tyrode solution and shaken in flasks with glass beads. It was then centrifuged at a low speed to remove the coarse particles, and thereafter at high speed for 1 hour. The deposit of trypanosomes was then resuspended

in Tyrode solution and washed several times. Finally a suspension of the washed trypanosomes was made in Tyrode solution of such a strength that 1 cc. contained about 2,000,000 trypanosomes.

For immunization the suspension was killed by adding 0·04 per cent. of formalin. The stock was divided into a number of tubes and kept at 4°C. Rabbits and a rooster were immunized by the injection of 1 cc. of the antigen every 2 or 3 days until 7 to 9 injections had been given. One rabbit was injected intraperitoneally and 5 rabbits and the rooster intravenously. The agglutination titre was determined at intervals, and after it had reached about 1 in 1,000 the subsequent 18 to 24 inoculations were made once or twice a week with living *T. cruzi* suspensions. The agglutination titres are shown in a table.

Agglutination tests.—The serum of the animals to be examined was diluted with Tyrode solution. Each serological tube contained 0·5 cc. of diluted serum and an equal quantity of freshly prepared live *T. cruzi* suspension (over 2,000,000 trypanosomes per cc.) Care was taken to have an even suspension and to eliminate all clumps. The tubes were shaken and kept at 37°C. for 30 minutes when readings were made.

The following is the summary :—

"1. *Trypanosoma cruzi* on the medium of Novy and MacNeal grew luxuriantly and formed colonies. From such cultures desired amounts of micro-organisms were removed and used for serological and immunological studies.

"2. Anti-*cruzi* serum with a titer of over 1 : 260,000 was obtained in one instance by the injection of rabbits with washed trypanosome cultures. The first 7 injections consisted of formalinized antigen while the subsequent injections (10 to 30) were live suspensions of washed *T. cruzi*.

"3. *T. cruzi* antigen (culture) was agglutinated by the serum samples from animals infected with *T. cruzi* in dilutions of 1 : 256 to 1 : 1,024, but with the sera of animals infected with nagana or murrina, the maximum titer of agglutination was 1 : 32.

"4. The California strain of *T. cruzi* (cultured from *Triatoma protracta*) agglutinated with the anti-trypanosome sera of the Panama strain (cultured from *Triatoma geniculata*) in very high dilutions."

W. Y.

PEREIRA (C.). **Upon the Detection of *Schizotrypanum cruzi* (Chagas, 1909) Infection in Reduviid Bugs.**—*Volumen Jubilare Prof. Sadao Yoshida.* Osaka, Japan. 1939. Vol. 2. pp. 365–367. [Summary taken from *Vet. Bull.* 1941, Aug. Vol. 11. No. 8. p. 503. Initialled E. S.]

The lid of a 9 cm. × 3 cm. Petri dish is lined with filter paper. The bottom of a 3 cm. × 1 cm. dish is sealed with paraffin wax close to the side of the bottom of the larger dish, and is filled with water, in order to maintain a moist atmosphere.

A reduviid bug, suspected of carrying *Trypanosoma cruzi* may be transferred immediately after feeding to the filter paper lining. The lid may then be carefully inverted and placed over the dish. The bug will crawl about very slowly so that the drops of faeces fall separately to the bottom, where they remain undried till needed.

Material so obtained may be examined immediately for trypanosomes, or may be utilized for animal inoculation, vital staining or permanent preparations.

Martins (A. Vianna). Infecção experimental do "Triatoma arthurneivai" Lent e Martins, 1940, pelo "Schizotrypanum cruzi." [**Experimental Infection of** *Triatoma arthurneivai* **with** *Trypanosoma cruzi.*]—*Brasil-Medico.* 1941. Mar. 1. Vol. 55. No. 9. p. 131.

Lent, H. & Martins, A. V. reported finding in 1940 a new species of Triatoma in Minas Geraes to which they gave the name of *T. arthurneivai*. They caught several but found none infected naturally with *T. cruzi*. Fresh captures having been made, larvae at different stages were allowed to feed on a laboratory assistant who was infected with the chronic form of Chagas's disease. All of them became strongly infected with the trypanosome. *H. H. S.*

Dias (Emmanuel). Serviço de estudos das grandes endemias. Transmissão do "Schizotrypanum cruzi" entre vertebrados, por via digestiva. [**Transmission of** *T. cruzi* **among Vertebrates by the Alimentary Tract.**]—*Brasil-Medico.* 1940. Nov. 23. Vol. 54. No. 47. p. 775.

An adult cat was fed on infected camondongos and 17 days later trypanosomes were found in its peripheral blood. In the course of three months 35 or more of the rats were eaten and by this time, the cat's blood was swarming with the parasites. There is little, if any, doubt that cats and dogs which eat rodents and other small sylvan mammalia become infected and so become intermediaries from which human infection may occur. Also, animals, *e.g.* cats, may become infected by themselves devouring infected insects, or the smaller mammals which have infected themselves in this way. *H. H. S.*

Pifano (Felix) & Dias (Emmanuel). Parasitismo natural do morcego "*Carolia perspicillata*" por um "Schizotrypanum," na Venezuela. [**Natural Infection of** *Carolia perspicillata* **by a Trypanosome in Venezuela.**]—*Brasil-Medico.* 1940. Oct. 19. Vol. 54. No. 42. pp. 695–696.

The bat, *C. perspicillata*, was the first of the chiroptera to be found in the New World with blood flagellates. The authors have recently examined 30 specimens and found four to be harbouring trypanosomes in the leishmania stage readily seen in sections of the heart or stomach. Two of the four inhabited a cottage highly infested with *Rhodnius prolixus*. Xenodiagnostic tests proved positive with *R. prolixus*, *Triatoma maculata*, *T. nigromaculata*, *T. infestans*, *T. sordida*, *Panstrongylus megistus*, *P. geniculatus*, *Psammolestes arthuri*, *Cimex hemipterus* and *Ornithodorus moubata*. The protozoon was cultivable readily on NNN and Noguchi's medium by sowing with the blood of the bat or of animals experimentally infected, and laboratory animals, guineapig, dog, or camondongo, acquired infection from the insects or by inoculation with culture or by animal to animal passage. Work is to be undertaken to prove whether the flagellate is *T. cruzi*. *H. H. S.*

Martins (A. Vianna) & Tupynamba (Antonio). Sobre dois casos agudos de molestia de Chagas observados em Minas Geraes, Brasil. [**Two Acute Cases of Chagas's Disease in Minas Geraes, Brazil.**]—*Brasil-Medico.* 1940. Dec. 21. Vol. 54. No. 51. pp. 839–841.

The authors give details of two patients, males aged 16 and 46 years, who presented Romaña's sign. One acquired the infection in Grão

Mogol in the northern part of the State of Minas Geraes, the other in Luz, in the western part of the same State. Direct examination of the blood, even in thick drop, failed to discover any trypanosomes, but the examinations were not made for more than a month after the beginning of the attack. Xenodiagnostic methods, however, proved the suspicion which had been aroused by the history of unilateral palpebral oedema.

H. H. S.

MAYER (Martin) & PIFANO (Felix). O diagnostico da molestia de Chagas por intra-dermo-reacção com cultura de *Schizotrypanum cruzi*. [**An Intradermal Reaction in the Diagnosis of Chagas's Disease.**]—*Brasil-Medico*. 1941. May 3. Vol. 55. No. 18. pp. 317–319.

For obtaining the antigen for this reaction the authors allowed *Rhodnius prolixus* to feed upon a patient suffering from Chagas's disease; from the insect, guineapigs were infected and from the blood of one of these animals cultures of *T. cruzi* were obtained on NNN medium. The trypanosomes were drawn from the water of condensation with a pipette, washed three times with saline, centrifuged and emulsified in saline with 0·5 per cent. phenol. From this, "cruzin" was prepared in the same way as "leishmanin" from Leishmania.

This product was tested in six patients proved to be suffering from Chagas's disease. All gave a strong reaction with a local swelling as large as an almond and a surrounding inflammatory zone attaining a maximum in 48 hours. Another six were apparently healthy but had lived for some years in houses infested with Reduviidae; they did not show any trypanosomes in their blood. Five were negative, one gave a positive response and his infection was proved by xenodiagnosis. A third group consisted of twelve persons, six with malaria, five with anaemia and ankylostomiasis and one with phagedaenic ulcer and subtertian malaria. None of these gave a positive reaction. Of ten others from an Estate hospital, three gave a positive, two with anaemia and splenomegaly, and one with an ulcer of the leg. The last had lived in a reduviid infested house. Cruzin was also tested on five patients with leishmania infections. All gave negative results with the former, but strongly positive with leishmanin.

Cruzin would seem, therefore, to be of great use as a rapid diagnostic agent.

H. H. S.

MAZZA (Salvador), MIYARA (Salomon), BASSO (Germinal) & BASSO (Redento). Primer quinquenio de la investigación por la M.E.P.R.A. de la enfermedad de Chagas en la provincia de Mendoza. [**Five Years of Investigation of Chagas's Disease.**]—36 pp. With 19 figs. (3 maps). 1941. Mendoza. Universidad Buenos Aires: Misión de Estudios de Patalogía Regional Argentina (Jujuy).

MAZZA (Salvador) & others. Investigaciones sobre enfermedad de Chagas. Esquizotripanides. Manifestaciones eruptivas agudas en la enfermedad de Chagas (exantemas o roscolas). [**Acute Eruptions in Chagas's Disease.**]—*Universidad Buenos Aires: Misión de Estudios de Patología Regional Argentina (Jujuy). Publicación No. 51.* 1941. 74 pp. With 64 figs.

Mazza (Salvador) & others. Investigaciones sobre enfermedad de Chagas. Esquizotripanides (IIa nota). Esquizotripanides urticariformes. [**Urticarial Skin Lesions in Chagas's Disease.**]—*Universidad Buenos Aires: Misión de Estudios de Patología Regional Argentina (Jujuy). Publicación No. 52.* 1941. 31 pp. With 23 figs.

Mazza (Salvador) & Miyara (Salomon). Investigaciones sobre enfermedad de Chagas. Esquizotripanides (IIIa nota). Esquizotripanides eritematosas polimorfas. [**Polymorphic Erythematous Skin Lesions in Chagas's Disease.**]—*Universidad Buenos Aires: Misión de Estudios de Patología Regional Argentina (Jujuy). Publicación No. 53.* 22 pp. With 9 figs.

MALARIA.

Précis of Abstracts in this Section.

Russell and Rao (p. 642) found *Anopheles culicifacies* to be the principal vector of malaria in the Tanjore District, S. India.

Ogurtsova (p. 642) states that the principal changes in malarial coma are in the blood vessels, with secondary effects on the nerve cells. The capillary system is much richer in the cerebral cortex than in the white matter, so that the effects of blockage of vessels are much less in the cortex, but the rich blood supply provides a wider field for the toxic activity of the parasites. Malkiel (p. 643), however, states that in malarial coma there is widespread meningo-encephalitis, together with granulomata in the white matter of the cerebrum.

Bhattacharjee (p. 644) describes a case of cerebral malaria, with epileptiform convulsions but without fever. Sarkar (p. 644) records a case of malarial psychosis.

Most and Tewksbury (p. 644) describe the results of laboratory studies in cases of *P. falciparum* infection.

Nandi (p. 645) discusses the respiratory mechanism of tissues in the presence of plasmoquine.

Russell and Knipe (p. 645) report on the value of malaria control by means of insecticidal sprays in houses in the Madras area. The method is effective and the cost is less than that of antilarval work, but is high in relation to the economic level of the community. Chopra *et al.* (p. 645) report that the essential oil of *Artemisia vulgaris*, which grows abundantly in hilly districts of India, has insecticidal and larvicidal properties.

Malaria of monkeys and birds.—By experiments on monkeys Passmore and Sommerville (p. 646) found that the course and severity of primary attacks of malaria due to *P. knowlesi* and *P. cynomolgi* were not affected by dietary deficiencies.

Mulligan *et al.* (p. 646) report experiments from which they conclude that agglutination of sporozoites, derived from mosquitoes, is a specific reaction.

Dikshit and Ganapathi (p. 647) report that sulphathiazole is effective in the treatment of *P. knowlesi* infections of *Macacus rhesus*.

Mulligan *et al.* (p. 647) show that serum obtained from monkeys which have recovered from infections with *P. knowlesi* has a protective action in infections with that parasite, especially in monkeys whose lympho-macrophage system has previously been stimulated by infection with *P. cynomolgi*. The conclusion is that the defence mechanism against malaria involves the interaction of both cellular and humoral agencies. They (p. 648) found similar results with the use of extracts of malarial spleens in place of immune serum.

The same authors (p. 648) found that although *P. knowlesi* infection in *Silenus sinicus* is not so severe as in *S. rhesus*, it may be so if the spleen is first removed from *S. sinicus*. Immunity acquired by a first attack may be appreciably lowered by subsequent splenectomy. *S. sinicus* possesses high natural immunity against *P. cynomolgi*, which is but little altered by splenectomy. The greater the natural immunity, therefore, the more it is due to some inherent quality of body fluids or tissues. Acquired immunity is largely removed by splenectomy, but that part which is due to antibodies in the blood remains. In defence against malaria there are three factors: inherent quality of the host, cellular mechanism, and specific humoral factor.

Mulligan and Swaminath (p. 650) have found *P. inui* infection in a monkey in India for the first time.

Gingrich (p. 650) reports experiments on birds which lead to the conclusion that natural immunity is due to some factor other than phagocytosis, but that acquired immunity is due to active phagocytosis. He (p. 650) has produced a degree of immunity in canaries by means of a vaccine prepared from blood infected with *P. cathemerium*; this immunity is probably due to activation of the lympho-macrophage system.

Manwell *et al.* (p. 651) found that sulphapyridine is effective against *P. circumflexum* but not against *P. relictum* var. *matutinum* and *P. nucleophilum*.

C. W.

Russell (Paul F.) & Rao (T. Ramachandra). **Natural Malaria Infections in Some South Indian Anophelines, with Special Reference to** *A. culicifacies*.—*Jl. Malaria Inst. of India.* 1940. Dec. Vol. 3. No. 4. pp. 543–562. [28 refs.]

This is an analysis of the results of the dissection of 36,414 Anopheles during three years in the Pattukkottai Taluk, Tanjore District, South India. The authors have previously described the epidemiology of malaria in this area [this *Bulletin*, 1939, Vol. 36, p. 131]. With the exception of isolated infections in *A. subpictus* and *A. vagus* [this *Bulletin*, 1939, Vol. 36, p. 1005] infected Anopheles were all *A. culicifacies*. The sporozoite index of *A. culicifacies* was only 0·061 per cent., but this is apparently sufficient to account for average spleen and parasite indices of over 40 and 30 per cent. respectively.

Norman White.

Ogurtsova (A. S.). **Malarial Coma.**—*Nevropatologia i Psikhiatria* [*Neuropathology and Psychiatry*]. Moscow. 1940. Vol. 9. No. 1–2. pp. 42–46. [In Russian.]

The author analyses three fatal cases of malarial coma, using the observations for the elucidation of the pathogenesis of malarial

affections of the central nervous system. While the *post mortem* appearance of the organs revealed the malarial nature of the cerebral disorder, this had not been established clinically in any of these cases.

A detailed account is given of the changes found in the brain. Microscopical examination showed profound and diffuse changes in the whole cerebral tissue, manifested mainly in vascular disturbances of the capillary network and small vessels (thickening of the walls, desquamation of endothelium, impregnation of walls and blocking of lumen with pigment, haemorrhages). The circulatory disturbances produced parenchymatous changes in the nerve cells. Since the pathologico-anatomical picture in malaria generally points to progressive degenerative changes in the reticulo-endothelial system, leading to changes in its function, the author suggests that malarial coma is due to heavy invasion by parasites of the cerebral capillaries, accompanied by a general or local depression of the R.E.S.

The heavy impregnation of the capillaries with pigment reveals the difference between the vascularization of the different elements of the brain. While, in the white matter capillaries are scanty with few branches, in the grey matter they form a highly developed network. This difference determines some of the clinical manifestations and histopathological changes in malarial coma. Since compensations in the circulation are more easily affected in the cortex, haemorrhages and necrotic changes are absent in this region. On the other hand the greater extension of the capillary system in the cortex provides a wider field for the toxic activity of the parasites, which results in the diffuse affection of the grey matter and the grave symptoms observed in malarial coma.

The blocking of the peripheral parts of the vascular system with pigment, by causing stasis in the network, leads to a reduction of the blood pressure and diapedetic haemorrhages, resulting in cardiac weakness, which was a marked feature in all the cases observed.

C. A. Hoare.

Malkiel (B. P.). **Histopathological Characteristics of Malarial Encephalitis.**—*Nevropatologia i Psikhiatria* [*Neuropathology and Psychiatry*]. Moscow, 1940. Vol. 9, No. 1–2. pp. 47–56. With 9 figs. [In Russian.]

An account is given of seven cases of malarial coma with a fatal termination, five of which had subtertian, one subtertian and benign tertian, and one quartan malaria. The *post mortem* findings in the brain are described and discussed in detail, and the following conclusions are drawn :—

(1) In all the cases, parasites and pigment were present, while alterative, exudative and proliferative phenomena were observed both in the soft membranes and in the brain tissue : the pathological process in the cranial cavity, therefore, represents meningo-encephalitis of malarial origin.

(2) Granulomata found in malarial meningo-encephalitis show considerable resemblance to the nodular aggregations of glial and mesenchymal elements in other types of infectious encephalitis.

(3) Malarial coma is associated with the presence of widespread meningo-encephalitis.

(4) The granulomata—which are characteristic but not specific in malarial coma—comprise glia, Hortega's cells and other mesenchymal elements.

(5) The granulomata are localized chiefly in the white matter of the cerebral hemispheres, in the corpus striatum, the internal capsule, nucleus dentatus of the cerebellum, and sometimes in the subependymal region. They did not occur in the cortex of the cerebrum or cerebellum nor in the white matter of the latter.

(6) The course of malarial coma usually manifests a parallelism between the clinical and pathological processes. *C. A. Hoare.*

BHATTACHARJEE (Jagadish C.). **Cerebral Malaria—an Afebrile Case with Epileptiform Convulsions.**—*Indian Med. Gaz.* 1941. Mar. Vol. 76. No. 3. pp. 159–160.

A Nepali motor driver, aged 38, after driving 11 miles suddenly fainted. He was brought to hospital completely unconscious. Soon after admission he had an epileptiform seizure, characterized by tonic spasm of the muscles with conjugate deviation of the head and eyes to one side : this was followed by clonic spasm and then complete relaxation. The whole seizure lasted about three minutes. Similar fits recurred every 10 to 15 minutes. Blood films showed a heavy infection with ring forms of *P. falciparum*. He was given an intravenous injection of quinine hydrochloride 10 grains in 20 cc. glucose solution, with adrenalin. He died of exhaustion six hours after admission. *N. W.*

SARKAR (S. K.). **A Case of Malarial Psychosis.**—*Indian Med. Gaz.* 1941. Mar. Vol. 76. No. 3. p. 159.

A youth, aged 16, was brought to hospital mentally deranged. He had been ill with fever for four days. He was completely disoriented about time and place, and sometimes could not recognize his parents. He looked very ill. The day after admission to hospital his temperature rose to 104°F. Blood examination revealed the presence of a few *P. falciparum* rings. Treated with quinine he made a rapid and complete recovery. When he became rational he remembered nothing about his illness. *N. W.*

MOST (Harry) & TEWKSBURY (Margaret H.). **Laboratory Studies in the Falciparum Malaria of Drug Addicts.**—*Jl. Lab. & Clin. Med.* 1941. Mar. Vol. 26. No. 6. pp. 1034–1039.

Epidemiological and clinical studies of *P. falciparum* malaria among drug addicts in New York City, and the treatment of such cases, have been the subject of previous publications [this *Bulletin*, 1941, Vol. 38, pp. 174, 175]. The present contribution is concerned with laboratory studies of the clinical pathology of the condition. In half the cases there was considerable anaemia : macrocytosis was commonly observed, attributable possibly to insufficient diet or liver damage. The white blood cell count was normal in half the cases, and raised in most of the remainder ; monocytosis was not common. Two-thirds of the patients had hyperbilirubinaemia ; in these cases the van den Bergh reaction was of the direct immediate type. Serum albumin was reduced, and the albumin-globulin ratio was reduced or inverted : in some cases serum globulin was markedly increased. There was a high incidence of positive Wassermann reactions. Henry's flocculation test was positive in all of the 25 cases in which it was used. In many patients the amount of urobilinogen in the urine was increased. [See also this *Bulletin*, 1940, Vol. 37, p. 789.] *N. W.*

NANDI (B. K.). **Observations on the Respiratory Metabolism of Tissues in the Presence of Plasmoquine.**—*Jl. Malaria Inst. of India.* 1940. Dec. Vol. 3. No. 4. pp. 475–493. With 3 graphs.

This paper describes the oxygen uptake of guineapig spleen, liver, brain, blood and cell-free enzymatic extract of liver, in the presence of plasmoquine, as measured with Barcroft differential manometers. The stimulation of oxygen uptake was most marked in the case of blood : with a concentration of plasmoquine as low as 1 in 300,000 the coefficient of stimulation was 41 per cent. Normal tissues which destroy the least amount of plasmoquine suffer the highest respiratory stimulation. The phenomenon of stimulation of oxygen uptake by tissues in the presence of plasmoquine is an enzymatic (thermolabile) reaction : the decomposition of plasmoquine takes place mainly through thermo-stable systems present in the tissues.

N. W.

RUSSELL (Paul F.) & KNIPE (Fred W.). **Malaria Control by Spray-Killing Adult Mosquitoes. Second Season's Results.**—*Jl. Malaria Inst. of India.* 1940. Dec. Vol. 3. No. 4. pp. 531–541. With 4 figs. on 2 plates.

This is a continuation of the work in the village of Kasangadu, Pattukkottai Taluk, Tanjore District, Madras [this *Bulletin*, 1940, Vol. 37, p. 504]. In all, 548 buildings, housing 1,805 persons, were sprayed once a week for 29 weeks from June 1939 to January 1940. As before, the spray used was 19 parts kerosene and 1 part pyrocide 20. Seventy-six of the buildings were sprayed a second time each week. The only important modification of technique in the second year was the systematic spraying of the outside of each house under the eaves, before the house was entered : this appeared to trap mosquitoes inside. The amount of spraying mixture used was 0·300 litre per 10,000 cubic feet sprayed. The total cost worked out at just below one rupee per head of population per season. A near-by village, comparable in all respects, acted as a control. The beneficial effect of spraying is shown by spleen and parasite indices determined in November of each of the three years 1937 to 1939 : these November surveys were made just after the peak of the malaria season. The November spleen indices in Kasangadu were 67·8, 24·0 and 14·4 as compared with 54·5, 61·0 and 57·4 in the control village. The corresponding parasite indices were 57·1, 11·5 and 6·2 in Kasangadu as compared with 45·5, 52·0 and 47·5 in the control village. In February 1940, no parasites were found in 24 infants less than a year old in Kasangadu : in the control village 5 infants out of 22 were harbouring parasites.

The method is effective in greatly reducing malaria transmission. The cost is less than anti-larval work in the same area would be, but it is high in relation to the economic level of the community. *N. W.*

CHOPRA (R. N.), ROY (D. N.) & GHOSH (S. M.). *Blumea densiflora* **and** *Artemisia vulgaris* : **their Insecticidal and Larvicidal Properties.**—*Jl. Malaria Inst. of India.* 1940. Dec. Vol. 3. No. 4. pp. 495–498.

Blumea densiflora grows in North India at elevations of from 2,000 to 4,000 feet. Neither the aqueous, acetone nor kerosene extract

of the leaves exhibited any appreciable larvicidal or insecticidal properties that could be attributed to the plant. The essential oil of *Artemisia vulgaris*, which grows abundantly in hilly districts in India, has insecticidal and larvicidal properties comparable with those of kerosene; kerosene is a feeble insecticide though a good larvicide. *N. W.*

PASSMORE (R.) & SOMMERVILLE (T.). **An Investigation of the Effect of Diet on the Course of Experimental Malaria in Monkeys.**—*Jl. Malaria Inst. of India.* 1940. Dec. Vol. 3. No. 4. pp. 447–455. [11 refs.]

It has often been stated that malaria runs a more severe course in people who are ill-nourished and in poor health than in those who are well fed and healthy. As such statements are matters of opinion rather than the result of controlled experiments, the authors decided to make observations on the course of monkey malaria in well-fed and under-fed animals. Monkeys (*Macacus radiatus* syn. *Silenus sinicus*) were kept for varying intervals on two different diets. In the one there was a resemblance to a good human lacto-vegetarian diet as consumed by certain groups in N. India. It was based on whole wheat and contained liberal amounts of pulses, vegetables, fruits and milk. The other diet resembled that of poor rice eaters all over India. Its main ingredient was parboiled milled rice and only small amounts of pulses, vegetables and fruits, but no milk, were included.

The monkeys on the first diet put on weight and remained in excellent condition, while those on the poor diet lost weight steadily, some dying within 6 or 8 weeks. The majority, however, survived for 6 to 12 months and then died, after suffering for several weeks from diarrhoea associated with inflammatory or degenerative changes in the small intestine. The monkeys of the first group were active and playful, while those of the second group were listless and uninterested in their surroundings. The two groups were thus clearly differentiated. When animals in the two groups were infected with malaria by the injection of equal doses of parasites (*Plasmodium knowlesi* or *P. cynomolgi*) there was little if any difference in the reaction. The course and severity of the primary attacks of malaria were unaffected by the differences in the state of nutrition of the monkeys.

C. M. Wenyon.

MULLIGAN (H. W.), RUSSELL (Paul F.) & MOHAN (Badri Nath). **Specific Agglutination of Sporozoites.**—*Jl. Malaria Inst. of India.* 1940. Dec. Vol. 3. No. 4. pp. 513–524.

A preliminary note concerning sporozoite agglutination in the presence of different sera was published in June 1940 [this *Bulletin*, 1941, Vol. 38, p. 338]. Details of this and of subsequent work are now reported. Observations were made with sporozoites of *P. gallinaceum*; in *Armigeres obturbans, Armigeres kuchingensis* and *Aëdes albopictus;* with sporozoites of *P. praecox* in *Culex gelidus, theileri* and *whitmorei*, and with sporozoites of human malaria, probably *P. malariae*, in wild *A. fluviatilis*. Only salivary glands which contain large numbers of sporozoites are suitable for this work. Care must be taken to distinguish close packing of excessive numbers of sporozoites and true agglutination: pressure on the cover-slip enables this to be

done with ease. When the serum has a powerful action agglutination is apparent immediately after dissection: in high dilutions of less potent sera there is a time-lag. In the authors' experiments the observations were recorded within a time limit of 15 minutes.

The sera of many species of normal animals agglutinate sporozoites of *P. gallinaceum* in dilution of 1/16 normal saline but no normal serum diluted 1/128 caused agglutination. The serum of fowls with chronic or latent infections of *P. gallinaceum* agglutinated the sporozoites of this species in dilutions of 1/4,000, in most cases, and in one case in a dilution of 1/16,000. The serum of a *rhesus* monkey with a chronic *P. cynomolgi* infection agglutinated sporozoites of *P. gallinaceum* in a dilution of 1/128. Similar results were obtained with the serum of a *rhesus* monkey with a long-standing *P. inui* infection. The serum of a human patient with chronic malaria agglutinated sporozoites of *P. gallinaceum* in a dilution of 1/64: dilutions of normal human serum above 1/16 caused no agglutination.

Sera from sparrows with low grade infections of *P. praecox* agglutinated homologous sporozoites in dilutions up to, and over, 1/8,000.

The serum of a human patient long resident in a hyperendemic malaria locality agglutinated the sporozoites of human malaria in wild *A. fluviatilis* in dilutions up to 1/8,000, and the serum of another similar case in dilutions up to 1/4,000.

The experiments indicate that sporozoite agglutination in high dilutions of malarial serum is a specific reaction. *N. W.*

Dikshit (B. B.) & Ganapathi (K.). **Sulphathiazole in Monkey Malaria.**—*Jl. Malaria Inst. of India.* 1940. Dec. Vol. 3. No. 4. pp. 525–529. With 1 graph. [11 refs.]

The authors have tested the action of sulphathiazole in *Plasmodium knowlesi* infections in monkeys (*Macacus rhesus*) which, as is well known, invariably progresses in intensity up to the death of the animal. It was found that the oral administration of a single dose of half a gramme of the drug to monkeys with a moderate infection would bring about the disappearance of the parasites from the peripheral blood. Radical cures were obtained by giving three grammes during three days, the parasites disappearing from the blood in four to six days. *C. M. W.*

Mulligan (H. W.), Sommerville (T.) & Swaminath (C. S.). **Cellular and Humoral Agencies in Defence against Malaria.**—*Jl. Malaria Inst. of India.* 1940. Dec. Vol. 3. No. 4. pp. 563–579. [17 refs.]

The experiments recorded in this paper relate to attempts made to modify the course of *Plasmodium knowlesi* and *P. cynomolgi* infection in *S. sinicus* and *S. rhesus* by the administration of homologous serum obtained from monkeys which had recovered from infections or had been rendered hyperimmune. It was possible to modify *P. knowlesi* infection in normal *sinicus* and *rhesus* monkeys by the administration of immune serum to a slight extent in some cases only. No evidence was obtained of any modification of *P. cynomolgi* infection in *sinicus* monkeys nor of *P. knowlesi* infection in splenectomized *sinicus* monkeys. On the other hand there was definite evidence that administration of immune serum to *rhesus* monkeys infected with *P. knowlesi* definitely

controlled the infection, provided the lymphoid-macrophage system had been previously stimulated by a *P. cynomolgi* infection. It has been shown by several observers that *rhesus* monkeys which have recovered from *P. cynomolgi* infections are as susceptible to *P. knowlesi* infections as are normal monkeys, and this in spite of the fact that the *P. cynomolgi* infections bring about a hypertrophy of the lymphoid-macrophage system. The degree of the hypertrophy or stimulation of the system is in direct proportion to the intensity of the infection. If such monkeys with a stimulated lymphoid-macrophage system are inoculated with *P. knowlesi* this infection progresses to a fatal termination, as in normal monkeys. On the other hand, if immune serum is administered as soon as parasites appear in the blood, infection is controlled to such an extent that a high percentage of monkeys survive. The immune serum is thus definitely protective, the protection being most evident in those monkeys which had experienced the most intense *P. cynomolgi* infection, and thus the greatest stimulation of the lymphoid-macrophage system. The conclusion is that the defence mechanism against malaria involves the interaction of both cellular and humoral agencies. *C. M. W.*

MULLIGAN (H. W.), SOMMERVILLE (T.) & SWAMINATH (C. S.). **Attempts to control Malarial Infections in Monkeys by the Administration of Spleen Extracts.**—*Jl. Malaria Inst. of India.* 1940. Dec. Vol. 3. No. 4. pp. 581–590.

The experiments recorded in this paper are similar to those described in the paper just reviewed. They differ in that saline extracts of malarial spleens were administered intraperitoneally in place of the immune sera. The results are very much the same, and are compatible with the view that immune substances occur in the spleen as they do in the peripheral blood. There was no evidence that immune bodies were present in the spleen in very much greater concentration than they were in the blood. The monkeys employed were *S. rhesus* and *S. sinicus*, while the parasites were *P. knowlesi* and *P. cynomolgi*. As with the immune serum experiments, the most definite results were obtained with *P. knowlesi* infections in *rhesus* monkeys which had recovered from a previous *P. cynomolgi* infection and which could be presumed to have a stimulated lymphoid-macrophage system. *C. M. W.*

MULLIGAN (H. W.), SOMMERVILLE (T.) & SWAMINATH (C. S.). **The Effects of Splenectomy on Natural and Acquired Immunity in Monkey Malaria.**—*Jl. Malaria Inst. of India.* 1940. Dec. Vol. 3. No. 4. pp. 591–601.

In this paper the authors describe experiments on malarial infections due to *Plasmodium knowlesi* or *P. cynomolgi* in the monkey *S. sinicus* subjected to splenectomy. Infections due to *P. knowlesi* in normal monkeys vary from mild to severe. Most monkeys after inoculation develop a mild infection followed by spontaneous recovery, while about 28 per cent. acquire heavy infections causing death. Splenectomized monkeys react much more severely, as shown by the death in the primary attack of 11 of 13, while one of the two which survived the primary attack died from a relapse. At the same time the rate of

increase of parasites in the blood and the intensity of the infection were much greater than in normal monkeys. It thus appears that the splenectomized *S. sinicus* reacts to *P. knowlesi* infections much as intact *rhesus* monkeys do.

Infections due to *P. cynomolgi* in normal *S. sinicus* are mild and transient in most cases. Splenectomized monkeys are somewhat more susceptible, as evidenced by a greater intensity of infection (three per cent. of red cells infected in place of under one per cent.) but on the whole it can be concluded that the high degree of natural resistance to the infection is not influenced by removal of the spleen. In the case of splenectomy carried out from 11 to 178 days after the crisis it was found that with *P. knowlesi* infections relapses occurred which were more severe than the primary attacks in normal monkeys but less severe than primary attacks in splenectomized ones. It can be concluded that the immunity acquired by a primary attack is appreciably lowered but not entirely removed by splenectomy. When the same procedure was adopted for monkeys recovered from *P. cynomolgi* infection only 8 of 10 monkeys relapsed, but in these the infection was more severe than primary attacks in unsplenectomized monkeys and was comparable with the primary attacks in splenectomized monkeys.

From the results obtained it would appear that *S. sinicus* possesses a high degree of natural immunity to *P. cynomolgi* and, as this is hardly interfered with by the removal of the bulk of the lymphoid-macrophage system by splenectomy, it is dependent upon inherent unsuitability of the body tissues or fluids for the development of the parasite. The natural resistance of the monkeys to *P. knowlesi* is less than to *P. cynomolgi*, but most of it is removed by splenectomy, an indication that the ineffective natural immunity is dependent upon the lymphoid-macrophage system and not upon some inherent unsuitability of the tissue of the host. The conclusion can be drawn that the greater is the degree of natural immunity, the more is this due to some inherent quality of the fluids or tissues of the body and the less to the lymphoid-macrophage system.

It has already been shown that *S. sinicus* after recovery from *P. knowlesi* infections is highly resistant to superinfections, and that this is associated with well-marked hypertrophy of the lymphoid-macrophage system of the spleen as well as the presence of antibodies in the blood. Relapses produced by splenectomy were more severe than primary attacks in normal monkeys but less severe than those attacks in splenectomized monkeys. It can therefore be inferred that, though the acquired immunity is largely removed by splenectomy, that part of it which is due to the presence of antibodies in the blood remains. With *P. cynomolgi* infections there is little evidence of hypertrophy of the lymphoid-macrophage system, for the natural immunity is so well developed that little acquired immunity is necessary to overcome the primary attack. In accordance with this, removal of the spleen in recovered monkeys removes little acquired immunity, with the result that the relapse corresponds with primary attacks in splenectomized monkeys.

The general conclusion is that in defence of the organism against malaria there are three agencies at work—firstly an inherent quality of the host which is inimical to the development of the parasite ; secondly a cellular mechanism in the lymphoid-macrophage system, centred chiefly in the spleen : and thirdly a specific humoral factor acquired as the result of infection. *C. M. W.*

MULLIGAN (H. W.) & SWAMINATH (C. S.). **Natural Infection with *Plasmodium inui* in *Silenus sinicus* from South India.**—*Jl. Malaria Inst. of India.* 1940. Dec. Vol. 3. No. 4. pp. 603–604. [10 refs.]

In blood films of a young *Silenus sinicus* from the foothills of the Nilgiri Mountains in South India *Plasmodium inui* Halberstadter and Prowazek, 1907, was discovered. Previous records of this parasite are from Borneo, Java and Sumatra, this being the first occasion on which it has been found in India. Its discovery is all the more remarkable in that naturally occurring malarial infections of monkeys have been rarely detected in India, the most precise record being that of KNOWLES of the presence of *P. semnopitheci* in *Pygathrix* (*Semnopithecus*) *entellus* in Assam. Other less satisfactory records are discussed in the paper.

C. M. W.

GINGRICH (Wendell D.). **The Role of Phagocytosis in Natural and Acquired Immunity in Avian Malaria.**—*Jl. Infect. Dis.* 1941. Jan.–Feb. Vol. 68. No. 1. pp. 37–45. With 6 figs. [23 refs.]

When a canary is inoculated with *Plasmodium cathemerium* the parasites which appear in the blood after an incubation period increase steadily in number up to the height of the infection, when a crisis occurs followed by a rapid disappearance of the parasites. The daily reproduction rate is on an average 15 merozoites, but of these two-thirds fail to survive. This destruction was correlated by CANNON and TALIAFERRO with phagocytosis of infected red blood corpuscles in the spleen and liver. At the crisis there is a greatly increased rate of phagocytosis. The question arises as to whether the failure of two-thirds of the parasites to survive during the acute rise in the infection, an indication of a natural immunity, is due primarily to phagocytosis or to some other cause. To investigate this point the author devised a method of blocking the reticulo-endothelial system by daily intravenous injections into the canaries of red blood corpuscles of other birds. The red cells of one type could be safely injected for three days. If continued beyond this *in vivo* agglutination of the injected red cells is liable to occur. If it was necessary to continue blockage another type of red cell had to be injected for the next three days. Blocking the cells in this manner during the incubation period or during the acute rise in the infection did not produce any change in the rate of increase of the parasites, whereas blocking carried out during the crisis or immediately after it tended to hinder the crisis and prevent recovery. If carried out during the latent period following the crisis the blockage favoured relapses. It would seem, therefore, that natural immunity as evidenced by the failure of numbers of parasites to develop during the acute rise in the infection is due to some factor other than phagocytosis. On the other hand the acquired immunity leading to the crisis and recovery is due to active phagocytosis, as this can be interfered with by blockage of the phagocytic cells.

C. M. W.

GINGRICH (Wendell D.). **Immunization of Birds to *Plasmodium cathemerium*.**—*Jl. Infect. Dis.* 1941. Jan.–Feb. Vol. 68. No. 1. pp. 46–52. With 1 fig. [16 refs.]

With the blood of canaries infected with *Plasmodium cathemerium* vaccines were prepared in two ways. In one a 50 per cent. suspension

of red cells from infected blood was exposed to 1 per cent. neutral formalin in a closed ampoule for 30 minutes, after which the formalin was removed by washing the red cells four or more times. In the other a suspension of unwashed red cells in an ampoule was kept in a water bath at 50°C. for ten minutes, after which the cells were washed four times. Either of these vaccines injected intravenously in 12 daily doses of 1 cc. (40–60 per cent. of the red cells injected) produced a high degree of immunity as demonstrated by the low grade infection and early recovery following intravenous inoculation of large numbers of living parasites. This immunity was not, however, as great as that following natural infections, for the inoculated parasites increased slightly in number for two or three days. In birds recovered from infection there was no such increase in the number of parasites injected. With smaller doses of vaccine the immunity was less marked. Vaccines prepared with normal uninfected blood, though not influencing the development of infection following inoculation, tended to favour recovery after the crisis. It was considered that this effect was due to an activation of the lymphoid-macrophage system leading to a more intensive phagocytosis of the infected cells when the infection had reached its height.

C. M. W.

Manwell (Reginald D.), Counts (Ellen) & Coulston (Frederick). **Effect of Sulfanilamide and Sulfapyridine on the Avian Malarias.**—*Proc. Soc. Experim. Biol. & Med.* 1941. Mar. Vol. 46. No. 3. pp. 523–525.

Sulphanilamide has been shown by Coggeshall to be effective against *Plasmodium knowlesi* infection in monkeys but ineffective against *P. inui* in the same animals. As regards human malaria reports are conflicting but it would appear that the drug and its derivatives are of little value. Coggeshall found that there was no action on the avian parasites *P. lophurae* and *P. cathemerium*; Durand and Villain showed that the drugs had no effect on *Haemoproteus columbae*. The authors of the paper under review record experiments with these drugs and three avian species—*P. circumflexum*, *P. relictum* var. *matutinum* and *P. nucleophilum*. The drugs were given in suspension either intraperitoneally or intravenously. It was found that only one of these parasites was affected. This was *P. circumflexum*, which was markedly susceptible to sulphapyridine. This drug was capable of preventing the appearance of parasites in the blood and of causing their rapid disappearance after they had appeared. It was, however, less active than plasmoquine, atebrin and quinine. It was possible to detect changes in the larger schizonts, which stained abnormally and showed irregularities in nuclear division.

C. M. W.

BLACKWATER FEVER.

Précis of Abstracts in this Section.

In the Jalpaiguri Dooars Das Gupta (p. 652) reports that blackwater fever is prevalent in and after the rainy season. Local natives are almost immune, but immigrants are commonly attacked, and the disease is particularly fatal in young children.

HUA and CHENG (p. 652) report blackwater fever from Hong Kong, and CHEN-WONG (p. 653) from Kunming.

TOONE (p. 653) reports a case of blackwater and discusses the hypotheses which have been advanced to explain the massive haemolysis and renal insufficiency which occur.

VENKATACHALAM and RATNAGIRISWARAN (p. 653) report encouraging results in the treatment of blackwater fever with an extract of the root bark of *Cassia fistula*, a tree which grows abundantly in India and Ceylon.

BICK and DREVERMANN (p. 654) describe a method for the rapid alkalinization of urine by means of intravenous injections of sodium lactate and sodium bicarbonate solutions.

BUELL and METTIER (p. 655) discuss paroxysmal nocturnal haemoglobinuria and give details of a case. *C. W.*

DAS GUPTA (C. C.). **Blackwater Fever. Observations on Cases treated in the Jalpaiguri Dooars.**—*Calcutta Med. Jl.* 1941. Jan. Vol. 38. No. 1. pp. 25–38.

Jalpaiguri Dooars is one of the intense blackwater fever areas in India. This disease is responsible for a comparatively high mortality amongst the employees of the tea estates and other residents of the area. The present paper is based on the author's experience gained during the last twelve years in the tea-gardens of Jalpaiguri Dooars.

The majority of the cases were seen between August and December. The incidence is at a minimum during January to March, cases beginning to appear with the onset of the rains in April. The local population and coolies are almost immune, but the disease is prevalent amongst the Bengalee clerks, forest officers, tradesmen and skilled workers such as Chinese carpenters, who are immigrants to the blackwater areas. Why the local people and the tea garden coolies are practically free from blackwater fever requires investigation. The author considers the matter, without reaching any definite conclusion.

The disease occurs at all ages, but it is particularly fatal in young children. The majority of the cases were in people resident in the Dooars for more than five years.

The author passes to a description of the various hypotheses which have been put forward to explain the causation of the haemolysis in blackwater fever, but is unable to throw any light on the problem. The rest of the paper discusses the clinical course of the disease and its treatment. *W. Yorke.*

HUA (T. J.) & CHENG (S. Y.). **Clinical Report of Two Cases of Blackwater Fever from Chun Wan, New Territories (Hong Kong).**—*Caduceus.* Hong Kong. 1940. May. Vol. 19. No. 2. pp. 96–99.

Blackwater fever is extremely rare in Hong Kong, even among the malaria-infested population of the New Territories. The present note gives clinical descriptions of two cases admitted into hospital within a period of less than three weeks. Both patients were immigrants and not natives of the district; both had had repeated attacks of malaria in a district where malignant tertian infection is rampant. There is nothing unusual in the clinical accounts of the cases. *W. Y.*

CHEN-WONG (Z. C.). **Blackwater Fever in Kunming. Report of Three Cases.**—*Chinese Med. Jl.* 1941. Apr. Vol. 59. No. 4. pp. 387–388.

Subtertian malaria is prevalent in Yunnan, but hitherto no cases of blackwater fever have been reported from this province. In 1938, 41 cases of malaria (20 tertian and 21 subtertian) were admitted to the Kun Hua Provincial Hospital. Three of these patients developed blackwater fever and case reports are given ; they contain nothing out of the ordinary. *W. Y.*

TOONE (Elam C.), Jr. **Clinical Observations on the Renal Insufficiency in Blackwater Fever. Report of a Case.**—*Amer. Jl. Trop. Med.* 1941. Mar. Vol. 21. No. 2. pp. 217–221. With 1 fig.

Details are given of a case of blackwater fever and of clinical and laboratory observations on the extensive renal dysfunction.

The case report contains nothing new. In commenting on it, the author states that the clinical syndrome of massive haemolysis and renal insufficiency has probably the same pathological and physiological background as that seen in transfusion reactions, acute haemolytic anaemias and in intoxications or infections in which there is a sudden and extensive destruction of red cells. The actual pathological and physiological changes occurring in the kidneys have not, as yet, been satisfactorily explained. YORKE and NAUSS (1911), working with rabbits, advanced the hypothesis that the renal damage with the resulting oliguria or anuria was caused by the obstruction of renal tubules by haemoglobin casts formed in an acid medium aided by low filtration pressure. These conclusions were later supported by the work of BAKER and DODDS (1925) and DEGOWIN (1938). These observations on experimental animals could not always be confirmed in human subjects, and therefore cannot be considered as final. The real contribution of these workers, however, consisted of their demonstration of the fact that renal insufficiency could be prevented if the urine was kept alkaline. Another explanation for the renal changes was that of LONGCOPE (1913), who regarded the reaction as being anaphylactic in nature. KIMMELSTIEL (1938) observed the presence of an interstitial nephritis in certain infectious diseases, septicaemia, extensive cellular destruction such as burns, and with marked haemolysis, particularly after blood transfusions. All of Kimmelstiel's cases showed oliguria or anuria of an iso- or hypo-sthenuric type, and a rise of the non-protein nitrogen of the blood. Kimmelstiel attributed the renal damage to an allergic reaction due to split or altered proteins.

Toone considers that in the light of these studies it is best to assume that no adequate or complete explanation has been offered for the pathological physiology involved in renal insufficiency in blackwater.

W. Y.

VENKATACHALAM (K.) & RATNAGIRISWARAN (A. N.). **The Use of *Cassia fistula* in the Treatment of Black-Water Fever.**—*Indian Med. Gaz.* 1941. Apr. Vol. 76. No. 4. pp. 211–212.

Many years ago O'SULLIVAN BEARE claimed that the liquid extract of *Cassia beareana* was of value in the treatment of blackwater fever. As this tree does not grow in India or Ceylon, an investigation was

undertaken to discover if any of the indigenous species of Cassia could be utilized for the preparation of a therapeutically active extract. It was found that an extract prepared from the root-bark of *Cassia fistula* gave encouraging results. This tree grows abundantly all over India and Ceylon up to an altitude of 3,000 feet.

The extract was prepared as follows :—One thousand grammes of the powdered root-bark was exhausted with cold 60 per cent. alcohol by the reserved percolate process ; to the 800 cc. of percolate thus obtained was added 100 cc. of glycerine, and the total volume was made up to 1 litre by the addition of 60 per cent. alcohol.

This extract was distributed to various district medical officers for trial in cases diagnosed as blackwater fever. In all 27 cases were treated with the extract with only one fatal result. No untoward effects were noticed in any of the cases. The urine invariably cleared in three to four days after the administration of a total quantity of 12 to 16 fluid drachms, the doses given being generally ½ to 1 fluid drachm every four hours.

In view of these results the authors consider that this extract of *Cassia fistula* should be given a more extensive trial in the treatment of blackwater fever. [As the Editor of the *Indian Medical Gazette* states in a footnote, blackwater fever is a disease which seems to be particularly susceptible to cure by " infallible specifics." This is possibly because of the variability of the intensity of the attacks. He adds, however, that the present report is very much more convincing than the usual run of reports on blackwater fever specifics, and that the tabular statement of the cases, which he was unable to reproduce because of shortage of space, adds conviction to the report. Only one fatal case in a series of 27 is certainly much below the average mortality of the disease. It is unfortunate that there are no controls such as could have been obtained if alternate cases only had been given the extract.]

W. Y.

Bick (Marjorie) & Drevermann (E. B.). **A Method for the Rapid Alkalinization of Urine.**—*Med. Jl. Australia.* 1941. Feb. 22. Vol. 1. No. 8. pp. 223–225.

A rapid alkalinization of patients who have been given a transfusion of incompatible blood is important in the prevention of renal damage. Bushby *et al.* have already recommended the administration of 120 grains of potassium citrate by mouth. This produces an alkaline urine within 30 minutes. The authors, however, consider that the nausea produced by the salt is a serious objection to the method. Experiments were therefore carried out on normal subjects, in order to determine the intravenous dosage of sodium lactate or sodium bicarbonate solution necessary to produce an equally or more rapid alkalinization.

It was found that 10 cc. of a 2 M or 3 M sodium lactate solution caused an increase in the *p*H of the urine which, although maintained, took some time to develop ; 10 cc. of saturated sodium bicarbonate solution produced alkalinization within 15 minutes, but this was not maintained ; 20 cc. of an equal mixture of the two solutions produced in 12 subjects a urine which was alkaline within 15 minutes, the change persisting for at least 90 minutes. Only very slight changes were observed in the alkaline reserve of the blood, and no unpleasant symptoms were caused. All the subjects had previously been given 30 grs. of ammonium

chloride by mouth, to ensure that the changes in the *p*H of the urine should be entirely due to the intravenous injection.

Sterilization of the solutions containing sodium bicarbonate was effected by filtration, of the sodium lactate solution by autoclave or by filtration. *John F. Loutit.*

BUELL (Arthur) & METTIER (Stacy R.). **Paroxysmal Nocturnal Hemoglobinuria with Hemolytic Anemia (Marchiafava-Micheli Syndrome).**—*Jl. Lab. & Clin. Med.* 1941. June. Vol. 26. No. 9. pp. 1434–1439.

The syndrome of paroxysmal nocturnal haemoglobinuria was first described by MARCHIAFAVA and NAZARI in 1911. Since then a considerable series of other cases has been recorded by various observers, who have described the clinical, pathological and laboratory features which have established nocturnal haemoglobinuria as a specific disease.

In the cases so far reported, the disease occurred most frequently during the second and third decades of life and, following a protracted course, terminated in death. Haemoglobinuria was the predominant sign and occurred almost always at night, frequently accompanied by vague abdominal pains. The course of the illness is characterized by recurrent attacks of fever which are usually intermittent, a predisposition to venous thrombosis and phlebitis, and a slight icteric tint in the sclerae and skin ; haemosiderin and haemoglobin can be demonstrated in the urine, and in a few cases slight enlargement of the spleen was reported.

The blood changes are most striking. The red cell count is between 1 and 3 millions per cmm. As a rule the cells are slightly larger than normal, so that the anaemia is usually macrocytic ; in others, however, it is normocytic. The haemoglobin is reduced to between 18 and 50 per cent. of the normal. Hyperchromia is noticed in some cases and hypochromia in others. In all the cases recorded the anaemia was refractory to treatment. The resistance to hypotonic saline was within normal range ; spherocytes were not observed, but there was a persistent reticulocytosis. There was invariably a leucopenia with a relative lymphocytosis and a moderate thrombocytopenia. The sternal bone marrow showed hyperplasia of the erythropoietic elements.

The aetiology of the disease is obscure. In contrast to haemolytic anaemia, a familial predisposition apparently does not exist in nocturnal haemoglobinuria. DACIE and others (1938) were able to show that increased carbon dioxide tension was of critical importance for the production of haemolysis.

Details of a case of nocturnal haemoglobinuria which came under the authors' care are given. In discussing the case, the authors say that the diagnosis presented a considerable problem. There was anaemia, probably of haemolytic origin, accompanied by slight icterus and reticulocytosis. Many points were suggestive of pernicious anaemia, but the failure of the bone marrow to respond to liver therapy eliminated this possibility. The resistance of the red cells to hypotonic saline within normal range, the negative family history and the absence of an enlarged spleen excluded a diagnosis of haemolytic icterus. Studies of the urine during the patient's first hospitalization were inadequate, but during the second period she was in hospital, discovery of the nocturnal emission of haemoglobin led to a diagnosis of nocturnal haemoglobinuria with haemolytic anaemia.

No adequate explanation can be offered for the abnormal haemolytic mechanism in this patient. The observations of Dacie and others were confirmed. After adding the patient's washed red cells to her serum and to normal serum, a slight degree of haemolysis was observed. When the media were acidified with carbon dioxide the haemolysis was greatly increased. Heating the serum to 56°C. destroyed the haemolytic activity. It appears from these studies that the patient's red cells were sensitized to some lysin present in her own serum and in normal serum. The rôle that hydrogen-ion concentration of serum or plasma may play in the production of the lysin deserves further recognition.

W. Y.

KEILIN (D.) & HARTREE (E. F.). **Absorption Spectra of Haemoglobin in Solution and in Red Blood Corpuscles.**—*Nature.* 1941. July 19. Vol. 148. No. 3742. pp. 75–77. With 1 chart.

This paper is of a technical nature and must be consulted in the original by those interested. *W. Y.*

VENOMS AND ANTIVENENES.

Précis of Abstracts in this Section.

VAZ and PEREIRA (p. 657) show that the toxicity of the venom of *Bothrops jararaca* is greatly reduced by heating, and discuss the coagulating and proteolytic actions of this venom and the effect of heat upon them. TABORDA (p. 658) records his experiments on the effect of temperature on the toxic, clotting and proteolytic principles of *B. jararaca*. There is a distinct difference in the temperatures at which these principles lose activity. TABORDA and TABORDA (p. 659) have studied the proteolytic enzyme of the venom of *B. jararaca*.

FISHER (p. 659) reports success in the treatment of herpes simplex by means of injections of the venom of *Ancistrodon piscivorus*. PRADHAN and PATWARDHAN (p. 659) have used viper venom in the treatment of haemorrhage into the vitreous of the eye.

ROTTMANN (p. 660) discusses the analgesic effect of the venom of *Naja tripudians*, advancing the view that it is due to an inhibiting action upon granulation tissue which, in certain diseases such as tabes dorsalis, invades the nerves or nerve roots. He uses cobra venom in the treatment of apparently cured tabes and other forms of late syphilis. PARSONNET and BERNSTEIN (p. 661), however, state that cobra venom acts on the higher nerve centres to produce analgesia and have used it with success in the treatment of angina pectoris.

NITZESCU and STAN-SUCIU (p. 661) note a decrease in the vitamin C content of liver and suprarenal glands of animals killed by cobra venom.

FRAZER and STEWART (p. 661) show that a lethal dose of cobra venom is inactivated when mixed with a finely dispersed suspension of oil in water, provided that it is injected intravenously. The protein in blood plasma provides protection against the creaming which occurs if the injection is intraperitoneal, and which is followed by intoxication.

Junior and Arantes (p. 662) show that certain mineral waters in São Pedro possess antitoxic powers against the venoms of a number of snakes.

Linton and Sarkar (p. 662) report a case of cobra bite in which the patient was treated with antivenene and placed in an " iron lung," which maintained his failing respiration until the antivenene had time to act. The patient recovered, and the case demonstrates the value of the apparatus in providing prolonged artificial respiration.

Pern (p. 663) considers the use of potassium permanganate solution to be of definite value in the treatment of snake bite.

From experimental work Rao (p. 663) infers that the toxic effect of scorpion sting is due to some acid constituent of the poison, and has had success in treatment by means of subcutaneous infiltration with sodium bicarbonate solution round the sting, or even, in severe cases, by intravenous injection of the alkali.

Voss (p. 664) describes the symptoms of poisoning by the bite of *Latrodectus mactans*, and advocates treatment with antivenene.

C. W.

Vaz (Eduardo) & Pereira (Anibal). Ação hemocoagulante pelo veneno de *Bothrops jararaca*. [**Blood Coagulating Activity of the Venom of** *B. jararaca*.]—*Anais Inst. Pinheiros*. São Paulo. 1939. July. Vol. 2. No. 4. pp. 3–71. With 20 graphs. English summary. [10 refs.]

" 1. The toxicity of a milesimal solution of dry *Bothrops Jaracaca* venom, in an intravenous injection, is reduced about 20 times for the pigeon and more than 25 times (observations showed up to 50 times) for the rabbit, by means of heating the solution for 15 minutes at 65°C.

" 2. The hemo-coagulating activity of the milesimal venom solution is rapid, and can be demonstrated—in vitro, by making it act on horse plasma or on a solution of pure fibrinogen, or judging by the transformation of fibrinogen into fibrin ; in vivo, by determinations of the coagulation time, before and after injection.

" 3. The hemo-coagulating activity is reduced about 10 times by heating the solution at 65°C. for 15 minutes.

" 4. The proteolytic action of the milesimal solution proceeds more slowly than its hemo-coagulating action and it requires very much higher doses. It can be shown—in vitro, by keeping the coagulated tubes from 1 to 24 hours at 37°C. for the observation of the liquefaction of the fibrin clot ;—in vivo, by a series of determinations of the time of coagulation before and afterwards, at different times, in order to disclose the negative phase, which means, the increase in the coagulation time caused by the alteration of the fibrinogen.

" 5. The result of the in vitro test depends on two factors—protease of the venom and fibrinogen (or horse plasma), being of little importance whether, or not, physiologic salt solution has been added in the tubes, thus altering the concentration ; as concerns the proteolysis, addition of physiologic salt solution, which lowers the concentration, delays the liquefaction.

" 6. Heating for 15 minutes at 65°C. reduces the proteolytic action on plasma, in vitro, about 5 times, and about 60 times in vivo, judging by the negative phase.

" 7. Considering the minimum active hemo-coagulating doses in our experiments—0·0001 cc. of the milesimal solution of dry venom,

intravenous, intramuscular or subcutaneous, in a rabbit—the difference between the coagulating and the anti-coagulating doses (6 cc.) is at least 60,000 times, and between the coagulating and the toxic doses (10 cc.) more than 100,000 times."

[See also this *Bulletin*, 1936, Vol. 33, pp. 380, 381; 1937, Vol. 34, pp. 650–653; 1939, Vol. 36, p. 566.]

TABORDA (Laura C.). A influencia da temperatura sobre os principios toxico, coagulante e proteolitico do veneno da *Bothrops jararaca*. [**The Influence of Temperature on the Venom of** *B. jararaca*.]—*Mem. Inst. Butantan.* 1940. Vol. 14. pp. 167–180. With 3 graphs. English summary.

"Our experiments studying the effect of the temperature on the toxic, clotting and proteolytic principles of the *Bothrops jararaca* venom led us to the following results:

"1. That this effect depends on various other factors, besides those already stated by Vital Brazil and Rangel Pestana (quality of the venom, heating period and degree of dilution), that is:

(*a*) the method of dehydration of the venom, if in the drying oven at 37°C. or at low temperature and high vaccuum;

"(*b*) the pH of the water in which it has been dissolved;

"(*c*) the method of heating—if applying direct or indirect heat;

"(*d*) if the heating of the venom has been carried on in dry state or in solution.

"2. That the venom dehydrated in the drying oven at 37°C. and heated in dry state loses its activity completely only at 180°C.

"3. That the dehydrated venom in the drying oven at 37°C. and in 1 per cent. aqueous solution of bi-distilled water at *p*H 6·2 (as employed in all our experiments) is completely inactivated at 110°C.

"4. That, when in solution, the temperature effect influences the toxic clotting and proteolytic principles from 40°C. on, depending on the heating period.

"5. That the toxic principle is activated at 50°C. heating being ceased as soon as this temperature is reached; at 60°C. it undergoes a decrease and at 70°C. an abrupt drop occurs, no other alteration being observed until the boiling point.

"6. That the clotting principle activity drops suddenly at 60°C., at 70°C. a remarkable activation has been noticed when heated for 5 minutes.

"7. That the proteolytic principle is activated at 50°C. (5 and 10 minutes) and at the boiling point (15′ and 30′) and suffers a sudden drop at 70°C. It is more thermo-resistant.

"8. That a comparison of the effects of the temperature on these three principles shows a noticeable difference at the temperatures at which a sudden drop of their activity is observed, which makes us believe that these three principles are distinct entities. This fact will be better elucidated on determining the exact temperature at which each principle in the whole venom undergoes an abrupt decrease, as we shall show in another paper.

"We believe, however, that on account of the numerous factors that influence the effect of the heat on the venom, only a separation—our scope—we shall be able to secure exact data and also establish an identity or diversity of these principles."

TABORDA (Armando) & TABORDA (Laura C.). Protease do veneno da *Bothrops jararaca*. [**Protease of the Venom of** *B. jararaca*.]—*Mem. Inst. Butantan.* 1940. Vol. 14. pp. 181–195. With 9 graphs [13 refs.] English summary.

"All the activity optimums of the proteasis of the *Bothrops jararaca* venom in regard to the enzymatic rules have been determined, using venom dehydrated in the drying oven at 37°C., fresh centrifuged venom and non-centrifuged venom; the greatest activity has been noticed in the latter.

"The following results were obtained:

"1. The concentration optimum of the enzyme 0·01 per cent. and of the substrate (sodium-caseinate) 1 per cent.;

"2. the pH optimum 8;

"3. the temperature optimum 35°C.;

"4. the antiseptic optimum toluol;

"5. the proteolyse cinetic obeys the rules of Schütz, that is, the amount of digested casein is proportional to the square root of the time of digestion;

"6. the autohydrolysis of the caseinate used as a substrate, has been effected under the same conditions;

"7. a few specific activators and inhibitors of known proteasis have been studied; inhibition by HgCl, KCN and boiling, as well as activation by ascorbic acid as mucin have been secured;

"8. under the same conditions as for the proteasis of the venom, the optimum pH and temperature for the hydrolysis of the caseinate by trypsin and the pH by the pancreatin have been determined, a great analogy between the hydrolysis by the venom and the trypsin having been observed;

"9. on account of its optimum of activity, activation and inhibitions, the proteasis of the *Bothrops jararaca* venom belongs to the tryptasis type."

FISHER (A. A.). **Treatment of Herpes Simplex with Moccasin Snake Venom.**—*Arch. Dermat. & Syph.* 1941. Mar. Vol. 43. No. 3. pp. 444–446.

The author recalls the paper by KELLY on this subject [this *Bulletin*, 1939, Vol. 36, p. 568] and reports 11 cases in which the venom of the moccasin [*Ancistrodon piscivorus*], in two or three doses, each of 0·2 cc. of a 1 in 3,000 dilution, were injected subcutaneously one week apart. The lesions of herpes in these patients were in different sites, including the mouth, and all patients had been subject to recurring attacks over a number of years. The injections were usually successful in decreasing the number of recurrences or in modifying the severity of the attacks. *C. W.*

PRADHAN (K. N.) & PATWARDHAN (N. G.). **Viper Venom in a Case of Recurrent Haemorrhage in the Vitreous.**—*Indian Med. Gaz.* 1941. Apr. Vol. 76. No. 4. pp. 221–222.

A case is reported in which haemorrhage into the vitreous of one eye, due to syphilis, was twice diagnosed, with gross impairment of vision. Little improvement took place with antisyphilitic and other treatment until injections of viper venom were given. After a course of 8 injections, varying from 0·1 cc. to 1·0 cc. of 1 in 1,000 solution,

and spread over a period of 7 weeks, vision had improved to 6/12 and the ophthalmoscopic appearances were much better. The authors discuss the action of the venom, emphasizing its power to promote absorption of granulation tissue, to prevent haemorrhage through coagulative action and to cause absorption of blood clot through cytolytic action. *C. W.*

GRASSET (E.) & SCHAAFSMA (A. W.). **Antigenic Characteristics of "Boomslang" (*Dispholidus Typus*) Venom and Preparation of a Specific Antivenene by Means of Formalized Venom.**—*South African Med. Jl.* 1940. Dec. 28. Vol. 14. No. 24. pp. 484–489.

In this paper is reported precisely the same work as was recorded by the authors in *Bull. Soc. Path. Exot.*, 1940, Vol. 33, pp. 114–131, and abstracted, together with a previous communication on the venom of *D. typus* in the same journal, in this *Bulletin*, 1940, Vol. 37, p. 513. *C. W.*

ROTTMANN (A.). Wirkungsweise und Indikationsgebiet von Schlangengiften, insbesondere des Giftes der Brillenschlange. [**The Action and Therapeutic Use of Snake Venom, particularly of that of** *Naja tripudians*.]—*Deut. Med. Woch.* 1940. Aug. 16 & 23. Vol. 66. Nos. 33 & 34. pp. 897–900; 930–933. With 2 figs. [31 refs.]

The first part of this paper is a discussion of the pharmacological action of cobra venom, in which no new work is reported. It is pointed out that venom rich in neurotoxin, such as that of *N. tripudians*, has effective analgesic properties, but the author considers this to be not a direct action on the nervous system, but rather, in view of the fact that it is most effective in diseases characterized by granuloma formation (malignant disease, leprosy, tuberculosis), as an inhibiting action on the granulation masses which have invaded nerve fibres. In tabes dorsalis RICHTER has shown that there is specific granulation formation in the nerve roots and it is thought that this is the origin of the lightning pains and crises so characteristic of that disease. These views form the basis of the treatment employed. The author quotes the results achieved in the treatment of 50 patients: in 23 there was complete and lasting relief of pain, in 15 the symptoms were greatly relieved, in 9 relief was experienced but the treatment had to be continuous, and 3 cases were refractory.

This treatment is combined with arsenical treatment in patients with positive serological tests, and is particularly effective with pentavalent preparations.

It has been claimed that the simultaneous administration of cobra venom and iodine is dangerous, but the author claims that in proper dosage this is not so and that such a combination has, in fact, a considerable value in both treatment and diagnosis of parasyphilitic lesions. The initial doses are:—0·5 cc. cobra toxin [strength not stated] subcutaneously and, at the same time, 0·3 cc. of a 6 per cent. solution of Mirion intramuscularly. These are increased up to 3 cc. of each, but it is not disclosed at what intervals they are given. [Mirion is hexamethylenetetramine diiodide in gelatin, the proportion of iodine being 15 per cent.] In serologically negative cases this form of treatment may provoke a positive Wassermann reaction and thus reveal the true nature of the disease.

The author therefore advises that cobra venom should be used in the treatment of cured tabes or meningo-vascular syphilis, and of mesaortitis and cerebral syphilis, even if all tests are negative, and that in the diagnosis of activity in these conditions, venom with iodine is valuable. *C. W.*

PARSONNET (Aaron E.) & BERNSTEIN (Arthur). **Cobra Venom. Its Use in Stenocardia. Preliminary Report.**—*Amer. Jl. Med. Sci.* 1940. Nov. Vol. 200. No. 5. pp. 581–586. [14 refs.]

Cobra venom, acts, like morphine, on the higher nerve centres to produce analgesia, but it does not form a habit or produce mental depression; on the contrary it appears to have a stimulating action on mental efficiency and it widens the fields of vision. It is slow to act but has a cumulative effect. Though it depresses the respiratory centre there have been no reports of dangerous reaction even with doses five times as large as that considered as the safe starting dose. There is no evidence of danger to liver or kidneys.

The authors have treated five cases of angina pectoris when drugs other than morphine had failed to give relief. Satisfactory results were obtained in all, though the action of the venom was slow to begin. The dosage was: 5 mouse units intramuscularly as the initial dose, repeated on the following two or three days; after that the dose was given every other day and finally only once or twice weekly. The dosage may be increased if necessary to 10–15 mouse units. Details of the cases are given.

Cobra venom cannot relieve the pain of acute coronary thrombosis, but in angina pectoris these preliminary trials indicate that it is a valuable therapeutic agent. *C. W.*

NITZESCU (I. I.) & STAN-SUCIU (Martha). Das Kobragift und das Vitamin C. [**Cobra Venom and Vitamin C.**]—*Klin. Woch.* 1940. Oct. 26. Vol. 19. No. 43. p. 1112.

The authors injected 6 guineapigs, each with a lethal dose (0·4 mgm. dry venom per kilo.) of cobra venom. The vitamin C content of 100 gm. of liver and suprarenal glands was estimated immediately after death, and as controls 6 guineapigs of similar weight were killed. The average results were:—Controls, liver 25·7 mgm., suprarenal 117·2; envenomed animals, liver 10·9, suprarenal 51·4.

These results are similar to those which have been observed in animals injected with diphtheria toxin and in cases of acute infective disease. *C. W.*

FRAZER (A. C.) & STEWART (H. C.). **Inactivation of Cobra Venom by Finely Dispersed Emulsion.**—*Brit. Jl. Experim. Path.* 1940. Dec. Vol. 21. No. 6. pp. 361–366. With 2 figs.

The authors show that a lethal dose of cobra venom, mixed with a finely dispersed suspension of oil in water, is rendered innocuous provided that it is injected into animals by the intravenous route; if injected intraperitoneally it kills after a delay. Intraperitoneally the mixture creams, and the rate of creaming coincides with the rate of development of symptoms of intoxication. Soap stabilized emulsion will cream in saline solutions or acids, but if protein is added, protection can be demonstrated.

The cobra venom is probably inactivated by adsorption at the oil water interface, and if this mixture is injected intravenously the plasma provides protection to the emulsion ; this protection is not present on intraperitoneal injection. The details of the experiments and the preparation of the emulsions are given. *C. W.*

Junior (Favorino Prado) & Arantes (J. B.). Poder anagotoxico das aguas de São Pedro sobre alguns venenos ofidicos. [**The Anti-toxic Power of S. Pedro Waters against Snake Venoms.**]—*Mem. Inst. Butantan.* 1940. Vol. 14. pp. 157–165. [16 refs.] English summary.

"1. The alkaline-sulphurous water of the fountain 'Juventude,' in São Pedro, seems to show a distinct anagotoxic power in regard to the venom of the rattlesnake (*Crotalus terrificus*), of *Bothrops jararaca* and of *Micrurus corallinus*.

"2. The pigeon injected with a mixture prepared *in vitro* with 1 cc. of venom diluted in saline, and 1 cc. of water of the fountain 'Juventude,' resisted 2 DML of the venom of *Crotalus terrificus* and 1·5 DML of the venom of *Bothrops jararaca*.

"3. The pigeons injected with 4 DML of crotalic venom, 2 DML of bothropic venom and 1 cc. of the water of the fountain 'Juventude' survived longer than the test animals.

"4. This effect seems to be due to a oxido-reduction phenomenon of the venom, caused by the sulphidrilated compounds of the water.

"5. The water of the fountain 'Juventude,' after standing for 10 days and consequently losing its colour and characteristic odor, has not protected a pigeon injected with 2 DML of crotalic venom. After standing the water loses its anagotoxic power.

"6. The chloric-bicarbonated-sodaic water of the fountain 'Almeida Salles' seems to present weak anagotoxic power in regard to the examined ophidic venoms.

"7. The chloric-sulphurated-sodaic water of the 'Gioconda' fountain is destitute of anagotoxic power against the examined venoms.

"8. The mineral waters under examination were used within 48 hours after having been collected at the fountain."

Linton (R.) & Sarkar (Nasimuddin). **A Case of Snake Bite Successfully Treated with the Help of the "Iron Lung."**—*Indian Med. Gaz.* 1941. Feb. Vol. 76. No. 2. pp. 92–93.

The patient, a boy of about 12 years, was admitted to hospital with a history suggesting snake bite and with symptoms of poisoning by a snake of the colubrine group. In spite of antivenene his condition deteriorated, but although respiration had almost ceased and the pulse was imperceptible at the wrist, he was placed in the "iron lung." The respiration rate was adjusted to 18 per minute and very soon a quantity of fine froth was blown out from the mouth ; cyanosis disappeared and the pulse became full and strong. In the meantime more antivenene was given to a total of 110 cc. In 1½ hours the patient was able to answer questions and in 5 hours he was removed from the apparatus. In the next 24 hours he had some fever but rapidly recovered afterwards.

The "iron lung" is a means of giving prolonged artificial respiration during which antivenene has a chance to act ; it is therefore evidently

a most valuable adjunct to treatment, but the chief problem in snake bite, that of getting the patient to the hospital alive, still remains.

C. W.

PERN (Sydney). **Permanganate for Snake Bite.** [Correspondence.]—*Brit. Med. Jl.* 1941. Mar. 1. pp. 338–339.

The author does not agree with the commonly accepted modern view that potassium permanganate is useless as a treatment for snake bite. He quotes his experience of about a dozen cases in man and 5 in dogs and has used as strong a solution of permanganate as can be made in cold water, of which he injects several syringe loads under and around the punctures. He has never seen harmful effects from this treatment, but has observed rapid improvement where the symptoms were bad. There were no fatalities in his cases. [There is no information as to the types of snakes responsible, but the author writes from Ballarat, Victoria.] He makes a plea for the full scientific investigation of the method, remarking that potassium permanganate is regarded favourably by those who, like him, live among snakes.

C. W.

FELDBERG (W.). **The Action of Bee Venom, Cobra Venom and Lysolecithin on the Adrenal Medulla.**—*Jl. Physiology.* 1940. Dec. 20. Vol. 99. No. 1. pp. 104–118. With 9 figs. [11 refs.]

RAO (P. Krishna). **Treatment of Scorpion Sting.**—*Jl. Indian Med. Assoc.* 1941. Jan. Vol. 10. No. 4. pp. 154–155.

Scorpion poison is acid in reaction, and it is possible to render it neutral to litmus by the addition of alkali in proper proportion.

Experiments in rabbits showed that the poison, when neutralized with sodium bicarbonate solution and injected subcutaneously, produced no evidence of intense pain such as was seen in rabbits similarly injected with poison not neutralized. Neutralized poison injected intravenously did not kill, but poison not neutralized did so in smaller doses. If the unneutralized poison were injected either subcutaneously or intravenously and if sodium bicarbonate solution were injected into the same area, or into a vein, within 30 seconds, the rabbits did not show signs of intense pain, nor was the poison fatal, though in controls these effects were seen.

The author therefore infers that the toxic effect of scorpion sting is due to some material, acid in reaction, which may be rendered innocuous by the addition of alkali. For treatment he recommends that 1–2 cc. of 2 per cent. sodium bicarbonate solution be infiltrated subcutaneously around the sting. This may be repeated if necessary and the injections may be given at any time after the sting if the symptoms are present. In very severe cases intravenous injection of 10 cc. of a 5 per cent. solution may be given. He has treated 84 cases by these procedures and all recovered. He points out that in heating sodium bicarbonate may be changed to the carbonate, but that this does not affect its action [but there may be some danger in the use of large doses of sodium bicarbonate solution, sterilized by heat, for intravenous work, see this *Bulletin*, 1940, Vol. 37, p. 877].

C. W.

Voss (A. H.). **The Bite of the Black Widow Spider.**—*Clinical Med.* 1941. May. Vol. 48. No. 5. pp. 123–125. With 1 fig.

Latrodectus mactans has been reported from Europe, Australia, North and South America and Africa. The symptoms of poisoning from the bite of this spider commence from 15 minutes to several hours after the bite. There is severe pain at the site and the patient may adopt the characteristic attitude, bent forward and moving the legs with difficulty. Pain spreads to the lower abdomen, which gradually presents board-like rigidity sometimes mistaken for acute abdominal disease, and to the chest. Dyspnoea may be marked and perspiration is profuse. In spite of the potency of the venom the case mortality is probably about 5 per cent. only; in most cases recovery takes place in a few days, though numbness, tingling and general weakness may persist for some weeks.

The author reports 6 cases. In four treatment with morphine, calcium, magnesium sulphate (intravenously) or other drugs was not very satisfactory, but in two treated with specific serum the results were dramatic. He therefore recommends antivenene as the ideal treatment. [See also this *Bulletin*, 1935, Vol. 32, pp. 673, 914, 915; 1936, Vol. 33, p. 401; 1937, Vol. 34, pp. 728–731; 1939, Vol. 36, pp. 570, 571, 868; 1940, Vol. 37, pp. 516, 517.] *C. W.*

MISCELLANEOUS.

James (Clifford). **Clinical Medicine in the Solomon Islands.**—*Med. Press & Circular.* 1941. Mar. 19. Vol. 205. No. 12. pp. 231–234.

The island of Choiseul is 100 miles long by 20 wide and round the coast lies a swamp, fed by the 200 inches of rain falling in the year, and breeding Anopheles. In the early days native villages were built in the hills, for defence, but since the advent of white men fighting has ceased, the natives have been attracted to the coast for fishing and trade, and the population has been gradually depleted by malaria. With quinine treatment this depopulation has now been checked. The author notes that malarial nephrosis, due to the quartan parasite, is cured by quinine injections, that blackwater fever occurs, and that gallstones are common in association with enlarged spleens. The commonest disease is phagedaenic ulcer, and the author notes that "Buxton's line," drawn diagonally down through the Pacific, divides not only the non-malarial East from the malarial West, but also the non-phagedaenic East from the phagedaenic West, which suggests a causative relationship between the two conditions.

Tropical myositis occurs; appendicitis is not seen. Gonorrhoea is common and is the usual cause of sterility. Yaws is very prevalent.

For Europeans the author advises 5 grains of quinine daily as a minimum dose, to be increased if necessary, but never to be omitted. For the prevention of prickly heat he recommends the cutting down of fluids at midday in order that sweating should be diminished, and the use of a powder of boric acid 1 part, zinc oxide 2, and amylum 3 parts, or of a salicylic acid lotion. *C. W.*

CARMAN (John A.). **Mathari Mental Hospital, Kenya.**—*Nursing Times.* 1941. Feb. 15. Vol. 37. No. 1868. pp. 146–149. With 10 figs.

The Mathari hospital was originally built in 1906 and, like many old lunatic asylums, resembled a prison rather than a hospital. In 1932, improvements were started and to-day the hospital is one of the most tastefully laid-out and one of the best equipped in the country. It has been realized that many of the patients must live permanently in the hospital, and it has therefore been made as attractive as possible. Its growth and development will always be associated with the name of Dr. H. L. GORDON, the visiting physician.

There are 235 beds for Africans, 14 for Asiatics and 15 for Europeans, and the staff is fully trained and adequate. The patients are restrained but little, the maximum possible liberty being allowed to them; as much of their time as possible is occupied in domestic routine duties. Those who cannot be allowed much liberty spend their time in large open compounds under the supervision of experienced attendants. The results of treatment are excellent, under these conditions, especially in those in whom the mental upset has a toxic origin in some disease like malaria, dysentery or influenza. A committee of responsible persons, under the chairmanship of the District Commissioner, meets monthly to inspect the hospital; patients, especially women, are not discharged until this committee is satisfied that they will be properly cared for until able to take up normal life once more.

C. W.

KNOTT (F. A.) & LEIBEL (B.). **Prevention of Pyrexial Reactions in Intravenous Therapy.**—*Lancet.* 1941. Mar. 29. pp. 409–411.

Minor pyrexial reactions often occur as unexpected complications of intravenous therapy. These reactions tend to take the form of small outbreaks, and the solutions used are often sent back for sterility tests, but investigation has shown that failures in sterilization are very rare. The reactions are usually due to protein bodies in the solutions, and these may be dead bacteria, free bacterial proteins or traces of other proteins. Dead bacteria or their proteins may be found in sealed screw-capped bottles; it is therefore wise to filter solutions through Seitz discs and then through sterilized sintered glass filters (to remove fibres from the discs) before storage. But this process will not remove free bacterial proteins; it is therefore essential to use water distilled and delivered in a closed system to sterilized bottles which are immediately autoclaved and capped to prevent the entry of bacteria. Organisms may enter with the chemicals used but these may be eliminated by the Seitz filtration.

Detection of dead bacteria in sediments after centrifugation is a matter of simple microscopy, but for the estimation of protein the albuminoid ammonia figure should be calculated; pyrogenic reactions have been given by solutions of which this figure was from 0·005 to 0·025 part per 100,000.

Foreign protein, other than bacterial, may enter solutions from apparatus which has been cleaned and boiled in sterilizers used for dishes and instruments; the quantity of protein may be very small, but may be enough to produce pyrogenic reactions if large intravenous doses are given from these pieces of apparatus. Similarly, protein may

be found in cracks on the inside of rubber tubing, and may enter solutions passing through the tube. In wards little should be done except a thorough flushing with clean cold water or weak soda solution ; sterilization should be a laboratory procedure.

A further source of trouble may be the still itself, and if there is high albuminoid ammonia in water from the still, double distillation from glass should be carried out. "

Suspended particles of non-protein matter have not, in the authors' experience, caused much trouble, but cotton and other fibres may be found ; they are best avoided.

[For the serious effects of pyrogenic substances in the treatment of cholera, see this *Bulletin*, 1939, Vol. 36, p. 380.] *C. W.*

EARLE (K. Vigors). **Experiences with Sulphanilamide Derivatives in Some Tropical Conditions.**—*Brit. Med. Jl.* 1941. Mar. 29. pp. 476–478. [16 refs.]

Dengue is not as a rule favourably influenced by the sulphonamide drugs and the author points out the danger of reducing the leucocytes in a disease in which leucopenia is a feature. Good results may be expected in the early stages of lymphogranuloma inguinale, and some improvement may result even in the later stages. In ulcerative granuloma combined treatment with sulphapyridine and intramuscular fouadin has been satisfactory. Sulphanilamide is useful in tropical ulcer only in the very early stages [no mention is made of the local application of the drug].

In fungous diseases of the skin in which secondary infection with streptococci has taken place, the author has found it advisable first to clear up the streptococcal infection by means of sulphapyridine taken by the mouth. Secondary infections of tropical or " salt-water " ear, a fungous disease of the meatus, may be prevented by sulphonamides taken by the mouth, as may secondary infections of the lesions of yaws. Sulphapyridine is useful in both non-filarial and filarial lymphangitis ; in the latter it is again probably active against the secondary bacterial invaders. Cellulitis of suppuration due to the stings of venomous marine animals, and infected lesions caused by various arthropods respond to therapy with these drugs. The author has treated cases of beriberi with vitamin B_1 combined with sulphonamides by the mouth, with successful results. *C. W.*

EARLE (K. Vigors). **Bush-Tea Haematuria.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1941. Mar. 27. Vol. 34. No. 5. pp. 395–398.

" Bush-tea " is a home-made infusion of *Guaiacum officinale* (lignum vitae) prepared usually from the leaves, but sometimes from the bark or the wood, and used almost as a panacea in the West Indies, but in particular for rheumatic conditions and gonococcal infection. The wood contains α and β guaiaconic acids (70 per cent. or thereabouts), guaiacetic acid (11 per cent.) and guaiacic acid (in small amount) ; the constituents of the leaves are not stated, but a case is reported in which haematuria followed 24 hours after a draught of bush-tea made from the leaves. The symptoms may result from repeated small doses, very small in the highly susceptible. There may be complaint of lumbar pain, chills, even rigor, with malaise and passage of dark coloured, even black urine, or the last may occur without the

others. The urine contains red corpuscles, and granular and epithelial casts. The author suggests that where these effects are seen after small doses of the "tea," they may be, like the Italian "favismo," anaphylactic in nature. Alkaline and emulcent drinks are followed by cure in a couple of days, there is no report of a case ending fatally. Which of the constituents, singly or in combination, is responsible for the haematuria has not been determined. *H. H. S.*

BAYLEY (H. H.). **Treatment of Larva Migrans.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1941. Mar. 27. Vol. 34. No. 5. pp. 399–400.

In Barbados larva migrans is often found in children and adults who have handled the sand above high water mark. The larva travels about 2·5 cm. in 24 hours, leaving a typical burrow visible to the naked eye. Itching is intense. The method advised has been successful in curing the condition in a few days in all the patients so treated by the author.

"The skin is thoroughly dried and cleaned with alcohol. Cedar wood oil is used to clear the affected area which is then examined with the $\frac{2}{3}$ inch objective of a dissecting microscope. A good hand lens can also be used with advantage.

"The ends of the burrow must be carefully examined as it is here that the larva may usually be found. It stands out clearly as a white, spherical mass due to the presence of plasma which surrounds it. Having noted the position of the larva the skin is cleaned for operation and 2 minims of procaine 1 : 1,000 is used to desensitize an area half an inch in diameter with the larva in the centre. A cautery is then applied until a small burn is produced. Sulphanilamide, grains $7\frac{1}{2}$, is prescribed for two days: this helps the burrow to heal, as it has obviously been contaminated by bacteria and much of the itching is caused by this secondary infection. When the patient returns in three days' time a faint brown line and a small cautery burn are all that remain and no further treatment is necessary.

"Each burrow must be examined and wherever a larva is discovered the cautery has to be applied."

C. W.

RAHMAN (S. A.) & ZAIDI (M. A.). **Study on the Normal Polynuclear (Arneth) Count at Hyderabad-Deccan.**—*Indian Jl. Med. Res.* 1941. Jan. Vol. 29. No. 1. pp. 225–230. With 2 graphs.

One hundred and twenty healthy male subjects ranging from 15 to 45 years of age were examined. The average weighted mean of the polynuclear count was 2·432, with a standard deviation of 0·234. This average is less than the British standards of Cooke & Ponder (2·74), and Kennedy (2·628). The authors suggest that the deviation to the left as compared with the British standards is due to climatic factors, and in this they agree with Kennedy and Mackay who found an average weighted mean for British airmen in Iraq of 1·935. The total leucocyte count did not differ appreciably from the results obtained in colder climates, but the lymphocyte and eosinophil counts were higher. [In figure 2 the polygons ascribed to Cooke & Ponder and to Kennedy respectively should be transposed.]

W. P. Kennedy.

VRYONIS (George). **Studies of the Effect of Intravenous Administration of Liver Extract in Patients with Sickle-Cell Anemia : an Unusual Response.**—*Jl. Lab. & Clin. Med.* 1941. June. Vol. 26. No. 9. pp. 1470–1473. With 1 fig.

The treatment of sickle-cell anaemia is acknowledged to be unsatisfactory.

Four patients were studied, the blood was examined for ten to fifty days to establish range of spontaneous variation. Twenty cc. of liver extract were administered intravenously and thereafter daily counts were made of white and red blood cells and reticulocytes for fifteen to forty days. Additional counts were carried out in one case at twenty minutes, three, five and twelve hours after the administration of liver extract. These patients showed no response, but in one there was an unusual haemopoiesis.

The increase of erythrocytes before that of reticulocytes differed from what is observed in pernicious anaemia ; the volume index was slightly higher than normal, but this frequently occurs in sickle-cell anaemia when the reticulocytes are high. The independent appearance of the leucocytosis as well as erythrocytosis and the duration of the rise exclude the possibility of its being the result of redistribution. The conclusion is that these are the effects of intravenous injection, as previous administration of liver by the mouth or intramuscularly was without effect. *P. Manson-Bahr.*

FORMIJNE (P.). **Experiments on the Properties of the Extrinsic Factor and on the Reaction of Castle.**—*Arch. Intern. Med.* 1940. Dec. Vol. 66. No. 6. pp. 1191–1214. With 16 charts.

The first part of this paper records a series of experiments on the chemical and physical properties of the extrinsic haemopoietic factor present in meat. The potency of the meat extracts was assessed after the addition of normal human gastric juice by administering the mixtures orally to patients with pernicious anaemia ; the criteria of potency being stimulation of a maximum reticulocyte response, progressive increase in red cell counts and in haemoglobin concentrations.

Treatment of minced beef with alcohol in final concentrations of 70–80 per cent. resulted in potent extracts, but alcohol in a concentration of 96 per cent. destroyed the extrinsic factor. Fats and lipoids could be removed from beef extract by extraction with ether without loss of activity. The extrinsic factor passed through an ultrafilter. Precipitates formed by treatment of the extract with saturated ammonium sulphate were estimated to contain rather less than 50 per cent. of the active substance originally present.

The second part of the paper deals with the properties of incubated mixtures of meat extract and gastric juice. An attempt to prepare a saline solution suitable for parenteral administration, by extraction of the mixture with 70 per cent. alcohol and precipitation with 90 per cent. alcohol, resulted in an inert product, whether injected or given by mouth. Other experiments demonstrated that incubated mixtures of known therapeutic potency were inactivated by treatment with 70 per cent. alcohol, in spite of the concentrated filtrate being reunited to a saline solution of the precipitate so that the reconstituted fluid

contained all the substances originally present. Inactivation also resulted when an incubated mixture of meat extract, gastric and duodenal juice was extracted with 70 per cent. alcohol.

As the incubated mixtures of extrinsic and intrinsic factors are inactivated by treatment to which the anti-anaemic liver principle is resistant, the author concludes that no reaction occurs *in vitro*, and that the reaction between the two factors takes place only *in vivo*; the probable site being the intestinal wall. *L. J. Davis.*

TROWELL (H. C.). **A Case of Haemophilia in a Muganda.**—*East African Med. Jl.* 1941. Feb. Vol. 17. No. 11. pp. 464–465.

The author reports what is probably the first case of haemophilia in an African native to be recorded in the literature. The patient, a man of about 30 gave a history of excessive bleeding and of haemarthrosis after injury. There were marked signs of osteoarthritis in both knees and in other joints, but the patient was not obviously anaemic. The capillary resistance test was normal, the bleeding time was 2½ minutes, and the coagulation time was from 30 to 45 minutes. He stated that two of his brothers and a maternal uncle were bleeders.

C. W.

WATSON (Malcolm). **Some Modern Problems of Tropical Hygiene.**—*Practitioner*. 1941. June. Vol. 146. No. 6. pp. 353–360. [14 refs.]

This is a general description, not only of the problems but also of the lines on which they have been attacked since the latter part of the 19th century, and includes a brief account of the principles of species sanitation and environmental control in malaria with which the author's name is so closely bound. Trypanosomiasis, brucellosis, yellow fever and nutritional problems are briefly reviewed, but the main theme of this short paper is that the problems should be viewed broadly and related to the whole life of the inhabitants of tropical countries, and that where research has been properly conducted, as in Malaya, Panama, India and the Dutch East Indies, great progress in tropical hygiene has been made. *C. W.*

MACGREGOR (R. G. Scott) & LOH (G. L.). **The Comparison of Basal Physiological Values in Racial Groups. Part I. Metabolism, Pulse Rate and Blood Pressure.**—*Jl. Malaya Branch Brit. Med. Assoc.* 1940. Dec. Vol. 4. No. 3. pp. 217–260. With 4 figs. [75 refs.]

The possibility of obtaining normal subjects belonging to diverse racial groups living in Singapore under the same climatic conditions offered an opportunity for investigation in which a certain basis for comparison could be achieved in a manner not possible when comparing averages derived from different sources under varying climatic conditions.

The racial groups selected for this investigation included only those from which it was possible to obtain a number of male subjects, between the ages of 18 and 30, who were willing to be investigated on at least four separate occasions, who exhibited a degree of physical

fitness, and about whose diet and habits detailed information was available. Subjects from the following eight groups were examined—European, Chinese, Malay, Javanese, Batak, Punjabi (Sikh), Punjabi (Hindu) and Tamil.

All subjects were conveyed to the laboratory by car after a night's rest and without food. Precautions were taken to prevent their indulging in any form of exercise on getting up, and on arrival at the laboratory they lay on camp beds and rested during the preliminary period. Strict supervision was made to ensure complete rest and quiet. Two basal metabolism measurements were made upon each subject on four separate days. The temperature, pulse rate and blood pressure were also measured with the subject in the basal and post-absorptive state. Of the two daily metabolism measurements, one was made between the first half hour and the first hour, and the other during the second hour. A third measurement was made if either was unsatisfactory. The basal metabolic rate (B.M.R.) was determined with a Benedict Recording Spirometer and a half-face mask was used in preference to mouthpiece and noseclip, as it was more comfortable. Control experiments were performed, using the Douglas-Haldane technique, and the results showed agreement between the two methods.

The mean values of the basal metabolism of the groups examined showed a depression below the standard found in a temperate zone for normal individuals of the same age and surface area in every case. The results can also be divided into two categories, according to the degree of depression of the B.M.R. in the different racial groups. In the European, Javanese, Batak and Sikh groups the depression was approximately five per cent. or more below the normal DuBois standard, whilst in the Chinese, Malay, Punjabi and Tamil groups the depression was approximately ten per cent. or more below the normal DuBois standard. A statistical examination of these results showed that a significant difference existed between the mean values of any two groups belonging to the separate categories—with the exception of the Punjabi group. (The basis for this assumption is that a significant difference exists when the difference between any two groups exceeds twice its standard error.)

No significant difference was shown to exist between the average pulse rates of different racial groups. The Sikhs exhibited the most rapid pulse rate, under basal conditions, and the Europeans the slowest, in spite of their basal metabolism being somewhat higher than most other groups.

The systolic pressure showed remarkably little variation in the groups examined, with the exception of the Sikhs. Allowance for the greater weight and surface area of this group reduced this difference to a certain degree. The same may be said of diastolic values and pulse rates which are closely comparable. It is quite clear that, where basal values are concerned, physically fit Europeans belonging to the age group investigated do not exhibit higher systolic and diastolic values than physically fit Asiatics; the average values in the European group examined were in fact slightly lower. Further investigations of this nature on some of the older age groups may be of interest in determining to what extent this relationship is maintained in normal individuals belonging to these races in later life.

In a comprehensive appendix, full experimental results are given in tabular form. *C. G. Warner.*

Robinson (S.), Dill (D. B.), Wilson (J. W.) & Nielsen (M.). **Adaptations of White Men and Negroes to Prolonged Work in Humid Heat.**—*Amer. Jl. Trop. Med.* 1941. Mar. Vol. 21. No. 2. pp. 261–287. With 2 figs. [19 refs.]

It is generally believed among cotton growers that in a hot environment the Negro has greater resistance to heat and greater capacity for work than the white man. The subjects in this study included 15 white men of whom 8 were members of the laboratory staff, ages 26 to 48, and 7 were sharecroppers in Mississippi of ages 18 to 21. There were 33 negro male subjects between 17 and 24 years of age of whom 11 were northern university students, 20 were Mississippi sharecroppers and 2 were Mississippi house servants. The negro students and the laboratory staff members were heavier than the sharecroppers. The negro sharecroppers averaged 282 cm.^{2} of body surface per kilogram of body weight as compared with averages of 277, 270 and 260 for the white sharecroppers, negro students and the laboratory staff respectively. Thus in dissipation of heat the sharecroppers had the advantage of somewhat greater surface exposure than the others.

Observations were made at Boston during spring, and later in Mississippi after two weeks or more of exposure to the warm, humid weather of summer. In each experiment the fasting subject, clad in trunks, socks and tennis shoes, walked two hours (if able to do so) on a motor driven treadmill at 5·6 km. per hour up a grade of 8·6 per cent. This work raises the metabolism to about 7 times the basal level and so demands an effective mechanism for heat dissipation in humid heat. All subjects were capable of walking for the full two hours in the cool northern laboratories, but several of the laboratory staff and both negro servants were forced to stop before the end of the two hours in the Mississippi experiments. All the sharecroppers walked for two hours easily. The environmental conditions under which the experiments were conducted were as follows. At Boston the experiments were made under ordinary laboratory conditions with dry bulb temperatures ranging from 15 to 25°C. and an average humidity of about 45 per cent. In Mississippi the dry bulb temperature ranged from 28 to 33°C. with an average of 30·5° and an average humidity of about 80 per cent. Under such conditions the subject's skin was wet with sweat within a few minutes after work started. Soon the trunks and socks were saturated and sweat began to drip on to the treadmill.

Observations were made of the heart rate throughout work and recovery by means of a cardiotachometer, of the blood pressure during the first 5 minutes of recovery, and of the rectal temperature before starting and at 15 to 20 minute intervals during work. In some of the experiments, once in the first hour and again in the second hour of work, surface temperatures at 11 points on the skin were measured by means of a thermocouple. Metabolism and lung ventilation measurements were made during various periods of the walk, together with determinations of weight loss and water intake. Blood sugar and lactic acid were estimated by standard methods and acetone was assessed by Rothera's qualitative test on samples of urine collected at 20-minute intervals during the first hour of recovery.

In addition to the indoor experiments described above 5 of the laboratory staff and 5 of the negro sharecroppers went through a 2-hour walk at about 6·7 km. per hour on an outdoor level course.

This required about as much energy as the indoor walk. In these experiments the skin, except for that protected by the trunks and socks, was exposed to the sun. Heart rate and rectal temperature were observed at intervals. On the days selected conditions were such that all the sweat evaporated on the skin. The subject bathed before the walk and was washed down with 5 litres of distilled water as he kneeled in a bath after completing the walk. The clothes were washed with the same water before it was sampled for analysis and determinations were made for chloride, nitrogen and urea concentration.

The experimental results for individual and group series of experiments are discussed in detail in the paper but the main conclusions may be summarized as follows. The two environments produced differences in the adaptations of the laboratory group to prolonged walking on the treadmill. The rate of sweating was twice as great after 10 days and 2⅛ times as great after 6 weeks in Mississippi as in the northern experiments. Body temperature remained within comfortable limits in the North but in most of the men it rose to intolerable levels in Mississippi. The marked elevation in the body temperatures of the subjects in the Mississippi experiments was due to limited radiation and evaporation imposed by the hot, humid environment. Heart rate followed closely the changes in rectal temperature until limiting values were approached. Some of the men were more efficient and performed the task with lower heat production in the hot environment than in the cool one. There was a progressive decline in efficiency during work, which tended to be more rapid at greater elevations of body temperature.

The negro sharecroppers who went through the experiments in the hot Mississippi laboratory maintained lower body temperatures than any other group studied, including those in the northern experiments. The white sharecroppers who were studied in Mississippi were less successful in regulating body temperature than the negro sharecroppers only because they were less efficient. When walking in the sun with skin exposed the negro sharecroppers were superior in temperature regulation to partially acclimatized white men of the laboratory staff.

During work the white sharecroppers had a higher rate of sweating than the Negroes—this was associated with their greater elevation of rectal and skin temperatures. Sweat produced by the negro sharecroppers during work contained lower concentrations of total nitrogen, ammonia and urea, and higher concentrations of chloride than the sweat of white men. Both negro and white sharecroppers drank water more freely than the laboratory group.

Mean values of R.Q. for the various groups during work in both environments were characterized by their close similarity. Blood sugar values were also very similar. Blood lactate was moderately lower in the northern experiments than in the South. *C. G. Warner.*

Hicks (C. Stanton). **The Australian Aboriginal. A Study in Comparative Physiology.**—*Schweiz. Med. Woch.* 1941. Mar. 22. Vol. 71. No. 12. pp. 385–388. With 5 figs. [17 refs.]

The research to be described was done among tribes within the tropics, within a radius of 350 miles west, north-west and south-west of Alice Springs in the centre of the continent. The resting metabolism

of the native in the post-absorptive state was measured by means of Benedict's Portable Field Metabolimeter and by gas analysis using the method of Douglas and Haldane. The results proved interesting in that, despite atmospheric temperatures of −4°C. in the early morning the naked subjects, lying on the ground beside the smouldering embers of their small camp fires, with no roof to shelter them, did not suffer any loss of heat such that increase in oxygen requirement resulted. The total number of natives investigated amounted to 160. Specific dynamic response to the ingestion of raw meat was also studied and the surface area of the natives was not only calculated from the data of Dubois and Benedict, but was assessed directly by the method of Takeys, using measured quantities of gummed paper strips with which to cover the body.

The metabolic investigations indicated that within a range of error of ± 10 per cent. there was no departure from the accepted Western European standards of metabolism, and this despite the fact that the conditions were, apart from the post-absorptive state and the immobility of the subjects, quite unlike those generally accepted as basal in the clinical sense, for the air temperatures were often exceedingly low, and the body naked. The respiratory quotient was found to be surprisingly low in many instances, but, since it was impossible to discover the dietetic history, the results of studies on the fasting and the meat-fed native were more illuminating. The metabolism of the fasting subject remained constant or tended to fall, whilst the R.Q. fell rather rapidly. This may well be due to the marginal nature of the nutrition of the subjects so far as calorific requirements are concerned. It is in harmony with their mode of life, which is one of conservation of energy, although when necessary they can be active and show great powers of endurance. The fact that their food is eaten raw for the greater part, that the whole animal is eaten, and that grubs are eaten alive, points to their vitamin intake being substantial. They show no signs of avitaminoses in a country where the white man quickly does so.

Measurements were also made of the skin temperature by means of thermocouples and the pulse volume at the wrist was estimated by the Sahli-Jaquet Volumbolograph. The results indicated that the walls of the radial artery contracted when the subject was exposed to cold, and that this contraction was part of a general vasoconstriction of the vessels leading to the hand. This conclusion was supported from observations on blood pressure during rapid changes in atmospheric cooling power produced by the passage of a cloud over the sun, in damp windy weather. Rapid rises of 30 mm. of mercury were consistently recorded, by two independent observers, in the systolic blood pressure of the naked native. Extremely small pulse amplitudes were not obtained unless the whole body was cold.

From theoretical considerations one would expect the skin temperature to be dependent more on environmental conditions than on body responses. Observations showed that in the same subject the average skin temperature could change as much as 8°C., a change out of all proportion to changes in skin temperature resulting from altered blood flow. Skin temperature was therefore used as an index of environmental conditions. When the white members on one expedition were compared with natives under similar conditions certain clearcut differences became manifest. The mouth temperatures of the natives fell, while those of the Europeans did not.

Certain facts have now been established with regard to the way in which the naked native is able to maintain his body temperature under extremely cold conditions. Quite regularly the native is exposed to air temperatures of 10–15°C., conditions which would be unbearably cold to a naked white, and would render sleep impossible. The authors are not yet able to state the effectiveness of the regulatory processes in the natives. In all cases low mouth or axillary temperatures were observed when the natives were exposed to cold. This, however, is attributable to other causes than a falling body temperature, and until it is possible to measure rectal temperatures no definite statements can be made as to constancy of body temperature under these cold conditions.

The native has an extremely active control of his skin circulation and heat loss from a cold part is minimized by a diminution of the circulation through that part. Moreover, it appears that this control is more definitely localized than is the case in the white. It is not implied that the circulation in any one part is independent of the temperature of the rest of the skin. Despite the cold environment the metabolism of the native does not increase. The responses of whites and natives under identical conditions have not as yet been compared in this respect, but there is no doubt that whites under conditions approaching those of the natives would show such a change. In association with this study it was of interest to observe that the natives experienced the subjective sensations of cold just as keenly as did whites. This was apparent during controlled cooling experiments, and often a native was seen to wake and sit up in his camp and build up a fire to warm himself.

The blood pressures of the natives were uniformly low compared with those of whites, and pulse rates over 60 were rare, the average being only a little above 50 beats per minute. The observation that the native is slow to raise his metabolism in response to cold is therefore not surprising and reveals an interesting distinction between the subjective sensations and the wakefulness associated with cold.

C. G. Warner.

REVIEWS AND NOTICES.

BURGESS (Perry) [President of the American Leprosy Foundation]. **Who Walk Alone. The Life of a Leper.**—318 pp. With 8 plates. 1941. London: J. M. Dent & Sons, Ltd., 10 Bedford Street, W.C.2. [12*s.* 6*d.*]

This book is exceptional in more ways than one. As a rule a "novel with a purpose" is either poor when regarded as a novel or inadequate for fulfilling its purpose. This book is successful in both aspects, and it succeeds because the main object—the portrayal of the life of a man who is unfortunate enough to contract leprosy—is kept to the front throughout, while the novel, the story behind it, is never permitted to thrust itself unduly into the limelight.

The author has for sixteen years been connected with the American Committee for the Eradication of Leprosy, five years as National Director and since 1930 as President.

It is said that at least thirty, perhaps more, American soldiers who served in the Philippines in the Spanish-American war became infected and were later admitted to a leprosarium, either at Culion or Cebu in the Philippines, or at Carville in Louisiana.

This book, *Who Walk Alone*, tells the story of one of these, the narration being embellished by the added experiences from other unfortunates in order to put before readers a composite picture; nevertheless, every statement of fact is authentic so that the whole is a true and genuine narrative. Some of those attacked had to leave wives and children or successful businesses which they had built up; this one, Ned Langford, was in this respect more fortunate in that, though engaged, he was not married and the business he was working up was not fully established. The author, though he has painted a dreadful picture of the suffering, mental and physical, which the disease entails and the poignant heartache of severance from and longing for one's home and kindred, is praiseworthily reticent on the more repulsive features of the disease. Branding a man with the name "Leper" has in the past led to his being regarded as a pariah, an outcast, as one already dead to the world. The reason of this is not easy to give, for leprosy is less infectious than is tuberculosis, and is less acute in its course; though horrible enough it is less disfiguring than some other diseases such as espundia (American leishmaniasis), and some forms of syphilis, nor is it congenital or hereditary, like syphilis.

The hero of the story, Ned Langford—if such a book can be said to have a hero, protagonist would, perhaps, be a better term—was sent with a draft to the Philippines and was in the island four years before returning on demobilization to America. While in the east he was billeted with a family in comfortable circumstances, in a good house, but two members of it developed leprosy some 7–8 months after Langford left the island.

Suspicion of his own infection was raised when he was severely burned in putting out a fire on his premises but felt no pain in part of the burnt area, and later when "spots," also painless, developed. He went to more than one doctor who failed to diagnose the condition until the patient himself had put them on the way. After nearly a year's treatment in New York without improvement he went to the Philippines again, to San Lazaro first and thence to the Culion leper colony. Culion is described and there are excellent photographs depicting the scenery and surroundings. Here everything was provided—housing, food, clothing, medical treatment—but, and this was the drawback and hardship of all leprosaria in the past, there was little or nothing for the inmates to do and they must have suffered unutterable boredom. In other words, what was needed to raise them from depression was work, at least occupation. This was found in gardening, after clearing of undergrowth, and in bringing water by pipe from a nearby spring. These undertakings kept him from despondency during his first two years of residence. From the start he had persevered with treatment, but he was one of the few unfortunates who made little if any progress. In two years he was again "unemployed" and there were 3,500 people in the Colony, at a loose end, condemned to idleness and *ennui* unless they could devise something to occupy them. He then instituted rules of agreement for a fishing contract by which each man drew a wage. This prospered and wages increased; those less affected by the disease worked at

the boats, others in more advanced stages attended to the nets. Many improved, and brooding, thoughts of suicide, madness and degeneration gave way to hopefulness, and a greater willingness to persevere with treatment. Later, larger schemes were undertaken and carried out, such as developing the colony's refrigerating plant, and the supply of electric light and power to the islanders in place of the old kerosene lamps, and provision of radios for the relaxation and amusement. "Work meant more than the filling of the hours and the earning of money, although it was good, too, to earn money—for a leper. What they learned gave them a trade, something to do in the world of the well, should they be paroled." The author gives the romantic story of the discovery of the curative drug, Chaulmoogra, and describes the scientific development of Culion, the provision of more hospitals on modern lines and of laboratories and opportunities for research.

A few words on the love story in the background. The discovery of his disease necessitates Langford's breaking off his engagement to Jane, his fiancée; meanwhile correspondence with Carita Nolasco, a girl of the family with whom he had stayed in the Philippines, and to whom he wrote "to improve his knowledge of Spanish," had ceased when she found that her family was infected. Later, he met her again and proposed marriage to her, but she refused him and when she became "negative" went away to look after paroled and returned uninfective lepers. Carita has a brother, Vicente, who tries to stir up strife and trouble in the Island, but dies in a typhoon. There is an amusing interlude which will appeal to those readers who have lived in the tropics, for something analogous is probably within the experience of most. Two persons agreed to share the progeny of a sow. There were 9 piglets. The owner claimed the odd one by "right of maternity," the other "by Napoleonic Law which gives the right to the father," *i.e.*, the owner of the boar which served her. Finally, on the advice of the magistrate, who, Solomon-like, suggested dividing it in two, they cut it in halves and used it all in a feast of celebration of the results of their litigation. All through his stay in Culion, Langford has a *fidus Achates*, Tom, who is companion and devoted servant. He marries, and Langford is left. After 25 years in Culion, during which time his disease slowly but steadily progresses, he obtains permission to return to America for admission to the Federal Leprosarium at Carville. At his journey's end he dies in the train from a heart attack.

We stated at the outset of this review that *Who Walk Alone* is exceptional in more ways than one. Other exceptional points are the provision of an index, and a very complete index, and an appendix of questions commonly asked by non-medical persons about leprosy. These questions are very appositely chosen and very adequately answered. The book gained the vote of the members of the American Booksellers' Association as their "Discovery of the Year" and we would like to endorse that opinion and wish it all success. *H. H. S.*

Printed under the authority of His Majesty's Stationery Office
By the South Essex Recorders, Ltd., Ilford.

(1685) Wt. P15/247 1,725 11/41 S.E.R. Ltd. Gp. 432.

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